# ESTERS OF MENTHOL
[A Revision]
by Charles August Mann

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## PREFATORY.

Thus far, only three esters of menthol, namely the acetate, the isovalerianate, and one in which menthol is combined with an acid of eight carbon atoms; have been found naturally in the peppermint oils[1]. Since the quality of the oil is influenced by the ester content, it is of some importance to study menthol esters. These are used in perfumery, but to a greater extent as medicines. Among these artificially prepared are the formate, the isovalerianate,[2] the carbonate[3] and the salicylate[4]. The menthol esters also offer excellent material for the studies in optical rotation on account of their large rotation. For these reasons the esters have been studied repeatedly but the results obtained do not always agree with those previously given. The object of this revision, therefore, is to bring together for comparison, these various results and to ascertain by experimental work which of the recorded data can be relied upon and to eliminate, as far as possible, those based on insufficient experimentation or incorrect observation.

1. Power and Kleber, Arch. d. Pharm. 232, p. 639-59
2. Bertram, Winther "Patente"der Org. Chem." Vol. 1, p. 623
3. B. Fischer, Die neuen Artzneimittel, 5 Aufl.1893, p.277
4. Bibus and Scheuble, C.C., 77, (2) p. 385.

## METHOD OF ANALYSIS USED BY WHEELER FOR THE DOUBLE SALTS.

The anhydrous salts were removed from the mother liquor

## MENTHYL FORMATE.

Synonyms:- Ameisensaeure Menthyl Ester.

History:- This ester which has not yet been found in nature was first prepared by Oppenheim[1] in 1861 while studying the stearopten of peppermint oil. In 1893 and in 1895, respectively, Schimmel & Co[2] prepared the formate on a commercial scale according to a modification of the method of Oppenheim patented by J. Bertram[3]. Later the formate was prepared and studied by Behal[4]. The last work on this ester seems to have been done by Tschugaeff[5] in 1898, who studied the optical rotation of the esters.

## FORMATION AND PREPARATION.

Formation. By condensation of menthol with formic acid.

$$C_{10}H_{19}OH + HOCHO = C_{10}H_{19}OCHO + H_2O.$$

Bertram[3] used hydrochloric, sulphuric and nitric acids as dehydrating agents. Behal[4] later used a double

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[1] Lieb. Ann. 120, p. 350.

[2] C.C. 1893 1, p. 985.

[3] Winther, Patente d. Org. Chem. Vol. 1, p. 623.

[4] A. Ch. 7, 20, p. 423.

[5] Ber. Dtsch. Ch. Ges. 31, p. 360-68, Ibid. 1775-80.

anhydride of formic and acetic acids prepared by himself, for the same purpose. Tschugaeff[1] not only used formic acid but also an excess of a formate and sulphuric acid. As to the temperature of reaction, Oppenheim[2] suggests a "mehr oder minder stark" temperature using a sealed tube. Bertram[3] claims that a low (niederer) temperature is preferable.

Preparation:- Bertram's method as patented is as follows:- "100 parts of menthol are mixed with 200-300 parts of formic (acetic, propionic, butyric, valerianic) acid with addition of 5-10 parts of sulphuric (nitric, hydrochloric) acid. The temperature must not rise above 25°C. otherwise hydrocarbons split off. This is diluted with water, the ester separated, washed with water containing soda and fractionated in a vacuum or with steam. The butyrate or valerianate can be heated to 70-80°C. The esters of the terpene alcohols find use in perfumes and as medicines. Trade names: Validol (valerianate), Stomachicum, Analepticum, Anticepticum."

Properties:- The properties of the formate, purified by fractional distillation, have been recorded as follows:

At ordinary temperature, menthyl formate is a

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1. Ber Dtsch. Ch. Ges. 31, pp. 360-68 and pp. 1775-80.
2. Liebig Ann. 120, p. 350.
3. Winther, Patente d. Org. Ch. Vol. 1, p. 623.

liquid, which, according to Schimmel & Co.[1] melts at 9°C. According to Behal,[2] menthyl formate boils at 219°, according to Bertram[3] at 95° under 10-11 m.m. pressure, and according to Tschugaeff[4] at 98° under 15 m.m. pressure. The density as given by Behal[2] is d =0.9499 and d =0.9396, according to Tschugaeff[4] 0.9359 at 20°.
The angle of rotation according to Behal[2] for the D line is -80.17°, according to Tschugaeff[4] -79.52° who gives the molecular rotation as -146.3°. Behal[2] gives the saponification number as 25.77.

From the above it becomes apparent that the properties of menthyl formate as recorded by these investigators and prepared according to as many modifications of the same general method, agree very well.

<u>Uses:</u>- Menthyl formate is a sure analepticum.[5] It is also an antinervosum, stomachicum and is used for sea sickness as a prophylactic.[6]

1. C.C. 1893, p. 985.
2. Ann. Ch. (7), 20, p. 423.
3. Winther Patente d. Org. Chem. Vol. 1, p. 623.
4. Ber. Dtsch. Ch. Ges. 31, pp. 360-68 and pp. 1775-80.
5. Kerner, Schimmel & Co. Ber. Apr. 1904, p. 107.
6. Köpke Schimmel & Co. Ber. Oct. 1904, p.107.

# MENTHYL ACETATE.

Synonyms:- Ger. Essigsaures Menthol, Essigsaeure Menthyl Ester.

History:- Menthyl acetate was first prepared by Oppenheim[1] in 1861. He assigns to it the formula:

$$\left.\begin{matrix}C_{10}H_{19}\\C_2H_5\Theta\end{matrix}\right\}\Theta$$

Its presence in the peppermint oil was first discovered by Power and Kleber[2] in 1894.

Occurrence:- Menthyl acetate occurs naturally in the oil of peppermint both in the American[2] and in the French[3].

Formation:- 1. By condensation of menthol with acetic acid.

$$C_{10}H_{19}OH + HOCOCH_3 = C_{10}H_{19}OCOCH_3 + H_2O.$$

It was according to this method that Oppenheim[1] first prepared this ester. He heated a mixture of menthol and acetic acid and a salt of acetic acid to 150°C.

2. By the action of silver acetate on menthyl iodide.

$$C_{10}H_{19}I + AgCOOCH_3 = C_{10}H_{19}OCOCH_3 + AgI.$$

The reaction goes on slowly when the iodide and acetate, covered with ether, are set aside for two days

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1. Lieb. Ann. 120, pp. 350.
2. Arch. d. Pharm. 232, p. 639-59.
3. Charabot, Bull. Soc. Chim. 19, p. 117.

more rapidly when heated. Berkenheim[1] 1892. As early as 1883, Arth[2] had already pointed out that when menthyl chloride is treated in like manner, no ester results, but menthene. This observation had been also corroborated by others. Berkenheim[3] also points out that menthene results when menthyl chloride is heated with potassium acetate.

3. By the action of acetyl chloride on menthol. Tschugaeff[4] 1898.

$$C_{10}H_{19}OH + ClOCCH_3 = C_{10}H_{19}OOCCH_3 + HCl.$$

4. By the action of acetic anhydride on menthol.

$$C_{10}H_{19}OH + (CH_3CO)_2O = C_{10}H_{19}OOCCH_3 + CH_3COOH.$$

This method was first applied by Tschugaeff[4] in 1898. Verley and Boelsing[5] state that an excess of the anhydride must be used, and Schimmel & Co.[6] emphasize that the mixture must be heated for at least an hour. This method, with the use of anhydrous sodium acetate is used for menthol assay of menthol containing oils.[7]

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1. Ber. Dtsch. Ch. Ges. 25, p. 686.

2. Jahres Ber. Der Ch. 36, p. 597.

3. Ber. Dtsch. Ch. Ges. 25. p. 686.

4. Ber. Dtsch. Ch. Ges. 35, p. 2477.

5. Ber. Dtsch. Ch. Ges. 34, p. 3356.
6. Schimmel & Co. Ber. Apr. 1910. p. 156.
7. U.S.P. 1910. p.318.

5. By the addition of acetic acid to menthene.

$$C_{10}H_{18} + CH_3COOH = C_{10}H_{19}OOCCH_3.$$

Suggested by Dr. Kremers, University of Wisconsin.

6. By treatment of menthyl urethane with acetic anhydride.

$$C_{10}H_{19}OOCNH_2 + (CH_3CO)_2O = C_{10}H_{19}OOCCH_3 +$$

This mehtod was used by Arth[1] in 1886.

Preparation:- The same general method of preparation of menthol esters patented by Bertram[2] as given under the menthyl formate, is applied to the acetate. The acetic anhydride method, used for assay purposes is also applicable to the preparation of smaller amounts.

Properties:-

The boiling points recorded by the several investigators are herwith tabulated.

| Temp. | Pressure. | Observer. | Date. | Reference. |
|---|---|---|---|---|
| 222-224° | ......... | Oppenheim | 1861 | Ann. 120, p. 350 |
| 220-225° | ......... | Berkenheim | 1892 | Ber. 25, p. 686 |
| 109° | 10-11 m.m. | Bertram | 1893 | D.R.P. 80711. |
| 228° | ......... | Power & Kleber | 1894 | A. d. Pharm. 232 p.639 |
| 108° | 15 m.m. | Tschugaeff | 1898 | Ber. 31, p. 364 |
| 116° | 22 m.m. | Patterson & Taylor | .... | J.C.S. 87, p. 33<br>Semmler V.3, p.47 |
| 11[illegible]° | 15 m.m. | Mann | | |

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[2] Winther Patente d. Org. Ch. Vol.1, p. 623.
[1] Ber. Dtsch. Chem. Ges. 19, Ref. 437.

The densities are herewith recorded in like manner.

| d. | Temp. | Observer. | Date. | Reference. |
|---|---|---|---|---|
| 0.9414 | .. | Berkenheim | 1892 | Centralb. 1893, p. 364 |
| 0.9185 | $\frac{20}{4}$ | Tschugaeff | 1898 | Ber. 31, p. 364 |
| 0.935 | $\frac{20}{0}$ | Kishner | .... | J.d.russ. Ch. Ges. 27,<br>Semmler Vol.3, p. 47 |
| 0.9307 | 13 | Patterson & Taylor | .... | J.C.S. 87, p.33 |
| 0.9230 | 20 | Mann | 1910 | |

The optical rotation observed is also tabulated herewith.

| Temp. | $(\alpha)_D$ | Observer. | Date. | Reference. |
|---|---|---|---|---|
| .... | $-72^{\circ}.15$ | Power & Kleber | 1894 | A. d. Pharm. 232, p. 639 |
| 20° | $-79^{\circ}.42$ | Tschugaeff | 1898 | Ber. 31, p. 364. |
| .... | $-79^{\circ}.26$ | Kishner | .... | J.d.russ.Ch.Ges.27, p480<br>Semmler, Vol. 3 p. 47. |
| 20° | $-72^{\circ}.42$ | Mann | 1910[1.] | |
| 20° | $-73^{\circ}.14$ | " | | |
| 24° | $-72^{\circ}.71$ | | | |

The only index of refraction recorded is that given by Patterson and Taylor which is $(n)_{D\ 98.1} = -155^{\circ}.6$ who also give a molecular refraction $(M)_{D\ 13} = -157^{\circ}.6$ That found by the writer at 20° with the Abbey Zeiss instrument is 1.4454

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1. These angles were taken on Mar.23, 1910, May 7, 1910, and May 29, 1911.

2. J.C.S. 87, p. 33. Semmler Vol.3, p. 47. Evidently incorrectly recorded.

From the data given it would seem that the ester ought to have a boiling point of about 223° at ordinary pressure of 109° at 10-11 m.m. pressure; a density $d\frac{20}{0}$ of 0.9185; a specific rotation $(\alpha)\frac{20}{D}$ of -79°.72 and an index of refraction $(n)_{20}$ = 1.4454.

The fact that the ester properties given by Power and Kleber[1.] are not in accord with the above might be explained by the fact that the ester was obtained from peppermint oil and no doubt was somewhat contaminated with other substances. Berkenheim's[2.] results, seem to be incorrect a fact which might be explained by knowing that menthyl chloride heated with sodium acetate decomposes in the same way as it does with potassium acetate, and these side products cause the difference in properties.

## Symmetric Menthyl Acetate.

Symmetric menthyl acetate was prepared in 1897 by Knoevenagel and Wiedermann[3.] who used the symmetric menthol which they investigated, and treated it with acetic anhydride. They obtained a compound which had a boiling point of 235-236°C. at 757 m.m. pressure.

## Menthyl Esters of Acetic Acid Derivatives.

Synonym:- Ger. Chlor-essigsäurementhyl Ester.

1. Arch. d. Pharm. 232, p. 639.
2. Ber. Dtsch. Ch. Ges. 25, p. 686.
3. Lieb. Ann. 297, p. 169.

This ester which is closely related to the menthyl acetate, was prepared in 1902 by Einhorn and Jahn[1] who warmed on a water bath a mixture of menthol, chlor-acetic acid, and sulphuric acid for 6 hours. Another method used by these investigators is that of boiling a solution of menthol in chloroform with chlor-acetic acid for three hours using a reflux condenser. The formula given to this ester is $CH_2ClCOOC_{10}H_{19}$. Its melting point is 38°C. Other compounds of the above type prepared by Einhorn and Jahn are the di-ethyl glycocoll menthyl ester and the camphoryl glycocoll menthyl ester. The first is prepared by allowing mono-chlor- acetic ester of menthol to react with di-ethyl amine. for 12 hours. Its boiling point at 20° is 160-162°. The hydrochloride melts at 108°, the methyl iodide addition product at 157° and the methyl chloride addition product at 185°. The formula given this compound is $N(C_2H_5)_2.CHCOOC_{10}H_{19}$. The camphoryl derivative is obtained by heating amino-camphor with the chlor-acetic ester of menthol at 80°C. The hydrochloride melts at 208°C.

In 1904 Bowack and Lapworth[2.] prepared several complicated esters which are referable to the acetic ester of menthol. The cyanacetic ester of menthol was prepared by heating menthol with the ethyl ester of cyanacetic acid

[1] Arch. d. Pharm. 240, p. 646.

[2] Jr. Ch. Soc. 85, p. 43.

when needles whose melting point is 83-84° are obtained. In a two per cent solution in benzene the rotation is -81°.12 The brom derivative $CNCHBrCOOC_{10}H_{19}$.is crystalline and has a specific rotation of -32°.9 The menthyl-p-tolylazo-cyanacetate $CH_3.C_6H_4.N=N.CH(CN)COOC_{10}H_{19}$ melts at 93-95°. The menthyl-p-brom- phenylazocyanacetate,

$$BrC_6H_4NH_2.CH(CN)COOC_{10}H_{19}$$

has a melting point of 97-98° and a rotation of -42°.75.

The phenyl acetic ester os menthyl prepared by Tschugaeff[1.] in 1898 and also by Cohen and Briggs[2.] later has a boiling point at 15m.m. of 197° according to Tschugaeff and 216° at 39 m.m. according to the second investigators. Tschugaeff gives for the density $d^{20}_{4}$= 0.9874 and a rotation of -69.57°

[1.] Ber. Dtsch. Ch. Ges. 31, p. 1778.

[2.] P. Ch. S. Nr. 254.

## MENTHYL PROPIONATE.

Synonyms:-Ger. Propion-saeure Menthyl Ester.

History:- In 1898, Tschugaeff[1] prepared this ester for studies on optical rotation.

Formation and Preparation:- 1. By the direct action of menthol with propionic acid.

$$C_{10}H_{19}OH + HOCOC_2H_5 = C_{10}H_{19}OOCC_2H_5 + H_2O$$

This is the general method of Bertram[2] who used an acid such as HCl to dehydrate.

2. By double decomposition between menthol and acid chloride of propionic acid.

$$C_{10}H_{19}OH + ClCOC_2H_5 = C_{10}H_{19}OOCC_2H_5 + HCl$$

Tschugaeff[1] digested these two substances on a water bath until no more HCl was given off. After purification the ester was fractionated.

3. By the action of the acid anhydride on menthol.

$$C_{10}H_{19}OH + O(C\ H\ CO)_2 = C_{10}H_{19}OOCC_2H_5 + C_2H_5COOH$$

Tschugaeff[1] also prepared this ester by the above means.

Properties:- The boiling point given by Tschugaeff[1] is 118° at 15 m.m., $d\frac{20}{4} = 0.9184$, $(\alpha)^{0}_{D} = -75.51$ and $M_{D} = -160.2$

### OTHER ESTERS RELATED TO MENTHYL PROPIONATE.

Phenyl di- rom propionsaeure Menthyl Ester was

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[1] Ber. Dtsch. Ch. Ges. 31, p. 360-68.

[2] Winther, Patente d. Org. Chem. Vol. 1, p. 623.

prepared by Cohen & Whiteley[1] who give it the formula,

$$C_6H_5CHBrCHBrCOOC_{10}H_{19}$$

and assign to it the melting point 84°C.

Beta- phenyl propion saeure menthyl ester ( menthyl propionic acid ester) $C_6H_5CH_2CH_2COOC_{10}H_{19}$ was prepared by Hilditch[2] in 1908 by treating beta-phenyl propionic acid and menthol with an excess of sulphuryl chloride and heating the mixture on a water bath but not over 120° until no more HCl is given off. The purified product crystallizes in prisms whose melting point is 28° and whose boiling point is 210-12° at 25 m.m. The density $d\frac{28}{4}$= 0.9836 and the index of refraction $n^{17}_{D}$= 1.5004.

Hilditch[2] also prepared menthyl propiolic acid ester ( Phenyl propiolen saeure menthyl ester),

$$C_6H_5C⋮C.COOC_{10}H_{19}$$

by heating at 140° for four hours menthol and propiolic acid with addition of HCl. Yellow crystals are formed which have a melting point of 33° and a boiling point of 235-238° at 30 m.m. The density, is $d\frac{33}{4}$= 1.0595 and the index of refraction at 17° is 1.5239.

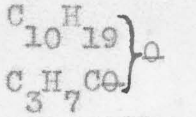
1. Jr. Ch. Soc. 79, p. 1308.

2. C.C. 79, (1) p. 837.

## MENTHYL n-BUTYRATE.

Synonym:- n- Buttersaeure Menthyl Ester Ger.

History:- Oppenheim[1] in 1861 prepared the buttyric acid ester of menthol to which he gave the formula



$\left.\begin{matrix}C_{10}H_{19}\\ C_3H_7CO\end{matrix}\right\}O$

In 1898, Tschugaeff[2] also prepared this ester among the others he prepared a this time.

Formation and Preparation:- 1. By the interaction of n-butyric acid with menthol.

$$C_{10}H_{19}OH + HOCOC_3H_7 = C_{10}H_{19}OOCC_3H_7 + H_2O$$

Oppenheim[1] prepared the ester by this method. Bertram[3] uses HCl for the dehydration agent in this method.

2. By the action of butyric acid chloride on menthol.

$$C_{10}H_{19}OH + ClCOC_3H_7 = C_{10}H_{19}OOCC_3H_7 + HCl$$

It was according to this method that Tschugaeff[2] prepared the ester.

Properties:- The boiling point of this ester is 230°-240° [1] at ordinary pressure or 129° at 15 m.m.[2] It is further described by Tschugaeff[2] as having a density of $d\frac{20}{4} = 0.9114$ and the rotation $-69^\circ.52$ and a molecular rotation of $-156^\circ.9$.

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[1] Lieb. Ann. 120, p. 350.

[2] Ber. Dtsch. Ch. Ges. 31, p. 360-68.

[3] Winther, Patente d. Org. Chem. Vol.1, p. 623.

## MENTHYL VALERATE.

<u>Synonym:-</u> Ger. Valerian-säure Menthyl Ester.

<u>History:-</u> In 1895, Bertram[1] in a German patent gave out the preparation of this ester. In 1898, Tschugaeff[2] prepared this ester.

<u>Occurrence:-</u> The iso-valerianate was found by Powers Kleber[3] to be present to a slight extent in the American oil of peppermint. Charabot[4] likewise records a valerianate in the French peppermint oils but does not specify which valerianate it is.

<u>Formation and Preparation:-</u> 1. By the action of valeric acid on menthol.

$$C_{10}H_{19}OH + HOCOC_4H_{11} = C_{10}H_{19}OOCC_4H_{11} + H_2O$$

Bertram[1] in 1895, heated these two substances together and used a mineral acid as dehydrating agent.

2. By the double decomposition between menthol and the acid chloride.

$$C_{10}H_{19}OH + ClCOC_4H_{11} = C_{10}H_{19}OOCC_4H_{11} + HCl$$

According to the above method Tschugaeff[2] prepared this ester.

[1] Winther, Patente d. Org. Ch. Vol.1, p. 623.

[2] Ber. Dtsch. Ch. Ges. 31, p. 360-68.

[3] Arch. D. Pharm. 232, p. 639-659.

[4] Bull. Soc. Chim. 19, p. 117.

<u>Properties</u>:- The menthyl n-valerianate of Tschugaeff[1] gave boiling point of 141° at 15 m.m., a density of $d^{20}_{4}$ = 0.9074, a rotation of -65°.55 and a molecular rotation of -157°.3. Bertram[2] finds that his ester has a boiling point of 125°-127° at 10-11 m.m. pressure.

<u>Uses</u>:- According to Bertram,[3] the isovalerianate is used in medicines. Kerner[4] and Köpke[5] prefer this compound over others as a prophylactic, against sea-sickness.

## OTHER ESTERS RELATED TO MENTHYL VALERATE.

Alpha-brom isovaleric ester of menthol was prepared in 1909 by Lüdy & Co.[6] who treated alpha-brom-isovaleric acid chloride with menthol and obtained a clear colorless syrup like liquid of boiling point 205°-208° at 760 m.m. which had a pleasant odor. It was soluble in alcohol, ether and chloroform and insoluble in water. It can be used as a nerve quieter.

[1] Ber. Dtsch. Ch. Ges. 31, p. 360-68.

[2] Semmler, Die Aethaerischen Oele, Vol. 3, p. .

[3] Winther, Patente d. Org. Ch. Vol.1, p. 623.

[4] Pharm. Centralb. 44, p. 917.

[5] Therap. Monatsb. 18, p. 296.

[6] C.C. 80, (1), p. 152.

# MENTHYL CAPRONATE.

Synonym:- Ger. n-Capronsäure Menthyl Ester.

History:- In 1898 Tschugaeff[1.] prepared this ester.

Formation and Preparation:- The menthol is heated on a water bath with the acid chloride as with the preceding esters. When carefully fractionated the boiling point is 153° at 15 m.m. pressure, the density is $d\frac{20}{4} = 0.9033$, the rotation $-62^\circ.07$ and $(M)_D = -157^\circ.7$

1. Ber. Dtsch. Ch. Ges. 31, p. 360-68.

## MENTHYL HEPTYLATE.

Synonym:- n- Heptylsäure Menthyl Ester, Ger.

History:- This ester was prepared by Tschugaeff[1] in 1898.

Formation and Preparation:- By the action of the acid chloride on menthol as in the preceding methods.

Properties:-The boiling point was found to be 165° at 15 m.m. pressure, the density $d^{20}_{4}$= 0.9006, rotation = -58°.85 and $(M)_D$ = -157°.7.

## MENTHYL CAPRYLATE.

Synonym:- Ger. n-Craprylsäure Menthyl Ester.

History:- The menthyl caprylate was first prepared by Tschugaeff[1] in 1898.

Formation and Preparation:-This was also prepared by the action of the acid chloride on menthol.

Properties:-The boiling point is given as 175° at 15 m.m. the density as $d^{20}_{4}$= 0.8977, the rotation as -55°.85 and $(M)_D$= -155°.8.

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1. Ber. Dtsch. Ch. Ges. 31, p. 360-68.

# MENTHYL STEARATE.

Synonym:- Ger. Stearinsäure Menthyl Ester.

History:-Menthyl stearate was prepared by Beckmann[1] in 1897.

Formation and Preparation:- Beckmann heated menthol and stearic acid anhydride for several hours at 160°-170°. The stearic acid anhydride was obtained by treating sodium stearate in benzene solution with phosphorus oxy-chloride and filtering off the sodium chloride. On evaporation of the benzene he obtained the anhydride. The melting point of the ester was found to be 39 °C.

[1] Jr. f. Pk. Ch. 55 (2), p. 14-31.

## MENTHYL ESTERS OF UNSATURATED ACIDS.

All of the esters of the unsaturated acids were prepared by Rupe[1] in 1903, which he used for the study of optical rotation.

Formation and Preparation:-All of these ester were prepared by the interaction of the acid chloride of the acid in question and menthol. The two substances were heated on a water bath until the HCl fumes ceased to come off. For every molecule of menthol he added two molecules of pyridine. The acid chloride was prepared as given under menthyl stearate.

The following esters were prepared by Rupe.

Crotonsäure Menthyl Ester
Alpha-beta-pentenesäure Menthyl Ester
Beta-gamma-pentenesäure Menthyl Ester
Gamma-delta-pentenesäure Menthyl Ester
Alpha-beta -hexenesäure Menthyl Ester
Beta-gamma-hexenesäure Menthyl Ester
Gamma-delta-hexenesäure Menthyl Ester
Delta-Epsilon-hexenesäure Menthyl Ester
Alpha-Beta-heptenesäure Menthyl Ester

Since only one person worked at these esters the properties are here ommitted since there is no means of disputing their correctness.

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[1] Ann. Ch. 327, p. 157-200.

## MENTHYL OF DI-CARBOXY ACIDS.

### MENTHYL OXALATE.

Synonyms:- Ger. Oxal-säure Menthyl Ester.

History:- Tschugaeff[1] prepared the menthyl oxalate in 1902.

Formation and preparation:- By heating together menthol and oxalic acid.

Properties:- A nice crystalline substance results whose melting point is between 67° and 68°. The rotation in benzene is -101°.5 and the boiling point at 12 m.m. is 225° It is decomposed on distillation.

Menthone is prepared from this ester by Bruni and Contardi[2].

### MENTHYL MALONATE.

In an article by Bruni and Contardi,[2] this ester is merely mentioned.

1. Ber. Dtsch. Ch. Ges. 35, (2), p. 2477.
2. C.C. 77, (2), p. 578.

# MENTHYL SUCCINATE.

Synonyms:- Fr. Succinate de Menthyle.

Bernsteinsäure Menthyl Ester.

## NEUTRAL MENTHYL SUCCINATE

History:-The neutral succinate of menthol (Fr. alpha éther neutre) was first prepared by Arth[1] in 1886 and later investigated by Tschugaeff[2] in 1902.

Formation and Preparation:- When two molecules of menthol and one molecule of succinic acid are heated in a sealed tube for 48 hours at 140°-150°, menthyl succinate results. This method gives the neutral ester.

Properties:- Crystallized from alcohol, it gives a melting point of 62° and boils at 220° at which temperature it decomposes into succinic acid and menthene. In benzene its rotation is -12°.20 and its specific rotation is -81°.52. The crystals are rhombic. Tschugaeff[2] states that the ester can be distilled without decomposition,-this no doubt under vacuum.

## MENTHYL ACID SUCCINATE.

Synonyms:- Ger. Bernsteinsäure Monomenthylester.

Fr. Beta Ether Acide.

[1] Ann. Chim. (6), 7, p. 479.

[2] Ber. Dtsch. Ch. Ges. 35, (2), p. 2477.

History: This ester was also prepared by Arth[1] in 1886.

Preparation:- Arth[1] obtained the ester $C_2H_4COOH.COOC_{10}H_{19}$, by heating menthol with succinic acid anhydride for 36 hours at 110°. A crystalline mass resulted which when purified and crystallized from alcohol had a melting point of 62°C. It was soluble in alcohol, slightly soluble in boiling water. In benzene it had a specific rotation of -59°.63 at a temperature of 20° for the D line. Sodium carbonate was decomposed by it to form the sodium salt. It also formed the calcium, barium, strontium, magnesium, potassium and silver salts.

## l-MENTHYL-l-TARTRATE.

Synonym:- Weinsäure Menthyl Ester.

History:- The only persons who worked on this ester and its derivatives are Patterson and Taylor[2] and Paterson and Kaye[3] in 1907.

Formation and Preparation:- The first prepared it by adding HCl to a mixture of ethyl tartrate and menthol at 120°-130°. Patterson and Kaye[3] prepared it by adding 50 gms. of the sodium ammonium tartrate to menthol and HCl in the cold and gradually increasing the temperature to 110°-130°.

Properties:- Fine needles resulted from crystallization

[1] Ann.Chim. (6), 7, p. 479.

[2] Proc. Ch. Soc. 21, p.15. [3] Proc. Ch. Soc. 22, p. 274.

from petroleum ether. Patterson and Taylor[1.] give to their ester the melting point 74°-75°; that given by Patterson and Kaye[2.] is 42° The respective densities given are $d_{5.5}$ = .1.0660, ($d_{\overline{100}}$ =0.9920) and $d_{\overline{16.3}}$ = 1.0450. The specific rotation as given by Patterson and Kaye[2.] is -76.11 at a temperature of 16°.3 for the D line, and $(M)_{D100^\circ}$ = -264°.20 and $(M)_{D5.5^\circ}$ = -287°.2.

Evidently the first work of Patterson's with Taylor[1] was not entirely satisfactory and therefore was continued by Patterson with Kaye[2.]

## MONO-1-MENTHYL-1-TARTRATE.

Synonym:- Ger. 1-Weinsaure Mono-1menthyl Ester.

History:- The acid ester of 1-tartaric acid was also prepared by Patterson and Kaye[2.]

Formation and Preparation:- This was prepared in the same way as in the previous experiment.

Properties:- Patterson and Kaye[2.] describe it as a crystalline substance obtained from water and with a melting point of over 200° and a specific rotation of -76°.46 at a temperature of 48°.6 for the D line.

## MONO-1-MENTHYL- I-ACETYL-1-TARTRATE.

History:- This ester was prepared by Patterson & Taylor[1.]

1. Proc. Ch. Soc. 21, p. 15. Jr. 87, p. 33.

2. Proc. Ch. Soc. 22, p. 274. Jr.

and by Patterson and Kaye[1].

Formation and Preparation:- The ester was obtained by boiling l-menthyl-l-tartrate with an excess acetyl chloride.

Properties:Paterson and Kaye[1] obtained crystals from dilute methyl alcohol whose melting point was 102.5° whose density was $d_{16^\circ} = 1.0550$ and whose specific rotation was $-70^\circ.28$. That prepared by Patterson and Taylor[2] gave a melting of 84.5°, a density of $d_{99.2^\circ} = 0.9915$, and $d_{14.4^\circ} = 1.0522$ and $(M)_{D14.4^\circ} = -258^\circ.9$.

1. Proc. Ch. Soc. 22, p. 274.
2. Proc. Ch. Soc. 21, p. 15.

1

## MENTHYL BENZOATE.

Synonyms:- Ger. Benzöe-säure Menthyl Ester.

Fr. Benzoat de Menthyle.

History: Menthyl benzoate was first prepared by Arth[1] in 1886 and by Beckmann[2] in 1887 and 1897. Other investigators are Bamberger and Lodter,[3] Tschugaeff;[4] and Zelikow.[5]

Formation :- 1. By the action of benzoic acid on menthol.

$$C_{10}H_{19}OH + C_6H_5COOH = C_{10}H_{19}OOCC_6H_5 + H_2O.$$

By heating these two substances together at a temperature of 170° for 488 hours, Arth[1] obtained the menthyl benzoate. The mixture was boiled with dilute sodium carbonate solution, extracted with ether and the ester recrystallized from alcohol.

Beckmann[6] similarly prepared the ester by heating in a sealed tube at 200°.

2. By the use of benzoic acid anhydride on menthol.

$$C_{10}H_{19}OH + HOCOC_6H_5 = C_{10}H_{19}OOCC_6H_5 + C_6H_5COOH.$$

This method was used by Beckmann and Pleissner who heat-

1. Ann. Chim. (6), 7, p. 479.
2. Jr. f. Pk. Ch. 55, (2), p. 14-31.
3. Ber. Dtsch. Ch. Ges. 23, p. 197-213.
4. Ber. Dtsch. Ch. Ges. 31, p. 360 and 1775-82. & 35,
5. Ber. Dtsch. Ch. Ges. 37, p. 1301.
6. Ber. Dtsch. Ch. Ges. 22, p. 912.

ed the mixture for 2-3 hours at 160° and purified as in the preceding method.

3. By double decomposition between benzoyl chloride and menthol.

$$C_{10}H_{19}OH + ClCOC_6H_5 = C_{10}H_{19}OOCC_6H_5 + HCl.$$

Tschugaeff[1] made use of this method and purified as above.

Uses:- By means of menthyl benzoate, menthol can be identified.[2] This statement is made by several other investigators.

Properties:- Menthyl benzoate forms prismatic crystals which can not be distilled without decomposition.[1, 3] Potassium hydroxide completely saponifies the ester[4].

The melting points recorded are here tabulated.

| M.P. | Observer | Date. | Reference. |
|---|---|---|---|
| .0° | Arth | 1886 | Ann. Chim. (6), 7, p. 479. |
| 53°-54° | Beckmann & Pleissner | 1887 | Ber. 22, p. 912. |
| 54.5° | Beckmann | 1897 | Jr.f.Pk.Ch. 55, (2), p. 16. |
| 55.5° | Mann | 1910. | |

The boiling points are as follows:

| B.P. | Pressure | Observer | Date | Reference. |
|---|---|---|---|---|
| 230° | ...... | Arth. | 1886 | Ann. Chim. (6), 7, p. 479 |
| 180° | 15 m.m. | Tschugaeff | 1898 | Ber. 31, p. 360 & p.1775 |
| 184° | 16 m.m. | Zelikow | ..... | Ber. 37, p. 1381.<br>Semmler, Vol. 3, p.48. |
| 301° | 740 m.m. | Zelikow | .... | " " |

1. Ber. 35, p.2477.
2. Ber. 22, p. 912.
2. Ber. 23, p. 179-213.
4. Ann. Chim. (6), 7, p. 479.

The rotations as recorded are here tabulated.

| Temp. | Angle | Observer | Date | Reference. |
|---|---|---|---|---|
| .... | -90°.92 | Arth | 1886 | Ann. Chim. (6), 7, p. 479 |
| .... | -86°.89 | Beckmann & Pleissner | 1887 | Ber. 22, p. 912. |
| .... | -90°.74 | Beckmann | 1897 | Jr.f.Pk.Ch. 55,(2) p.14 |
| .... | -90°.90 | Tschugaeff | 1898 | Ber. 31,p.360-68. & 1775 |
| 24° | -72°.71 | Mann | 1911. | |

The density is given by Beckmann and Pleissner[1] as 0.8312.

For $(M)_D$ Tschugaeff[2] gives the value -78°.0.

From these results it would seem that the melting point of menthyl benzoate ought to 54°, its boiling point at15 m.m. 180°, its density 0.8312, its rot ation in 20% alcohol -90°.91 and $(M)_D$ = -78°.0

It seems from the above that Arth's ester was impure because it differs so greatly from the others in the boiling point and the rotation. The rotation in most cases agree very well which would be an indication of the identity of the ester.

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[1] Ber. Dtsch. Ch. Ges. 22, p.912.

[2] Ber. Dtsch. Ch. Ges. 31, p. 360-68. & 1775-82.

## OTHER MENTHYL ESTERS RELATED TO THE BENZOATE.

In 1893, Hans Rupe[1] prepared the hydro-benzoic acid esters whose optical properties he studied. He obtained these by treating the menthol with the acid chloride in question.

In the following years Cohen with his students Briggs,[2] Raper,[3] and Armes[4] prepared the chlor, brom-, iodo- and nitro- benzoic acid esters also for the study of their optical properties. These were prepared in nearly every case by heating the acid chloride with menthol at 130°-140°

Somewhat earlier Tschugaeff[5] had also worked along this line.

The esters are of little importance except in the study of optical rotation.

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[1] Jahrsb. d. Forts. D. Ch. 56, (2) 797.

[2] Jahresb. d. Forts. d. Ch. 56, (2), p. 1493.

[3] Jahresb. d.Forts.. d. Ch. 1904, p. 1543-4

[4] C.C. 77, (1) p. 1697.

[5] J. fuss. phys. Ch. Ges. 34, p. 606.

## MENTHYL SALICYLATE.

History:- In 1906, Bibus and Scheuble[1] prepared this ester.

Fromation and Preparation:- These investigators heated to melting a mixture of menthol and salicylic acid but it was not allowed to reach 220° Through the liquid formed some gas was blown.

Properties:- The ester is a thick liquid of hardly any odor, with a sweet taste, of boiling point 190° at 15 m.m. or 175° at 10 m.m. It is insoluble in water but soluble in most organic solvents. It is used therapeutically.

Gadalowski[2.] in 1906 claimed that the ester of Bibus and Scheuble was made up not of menthylsalicylate but of a mixture of the two components which acts differently than do the components separately. He also claimed that the ester was menthol with the salegin radical. The ester prepared by Gadalowski decomposes with water at body heat, but that prepared by Bibus and Scheuble does not.

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1. C.C. 77, (2), p. 385.
2. C.C. 77, (2), p. 1623.

## MENTHYL CINNAMATE.

Synonym:- Ger. Menthyl Zimmtsäure Ester.

History:- This ester was prepared by Hilditch[1] in 1908.

Formation and Preparation:- Hilditch obtained this ester by treating menthol and cinnamic acid with sulphuryl chloride.

Properties:- An oil resulted which Cohn and Whiteley[2] describe as a yellow oil. Its boiling point was found to be 230°-233° At -15°C. it was still a liquid. The density was $d\frac{17}{4}$= 1.0079 and its index of refraction $n\frac{17}{D}$= 1.5433.

## MENTHYL-HYDRO-CINNAMATE.

Synonym:- Ger. Hydro-zimmtsäure Menthyl Ester.

History:- Tschugaeff[3] prepared this ester in ....

Properties:-This ester has a boiling point of 203° at 15 m.m. pressure, a density of $d\frac{20}{4}$= 0.9854, and a rotation of -52°.21

Besides the above esters, Cohen and Whiteley [2] have prepared the alpha-menthyl-zimmtsäure-menthyl ester $C_6H_5CH_2.CH(CH_3)COOC_{10}H_{19}$ whose melting point is 50°, whose rotation is -20°.44, in a 30°.48 m.m. tube at 58°C.; and the alpha-methyl-hydrozimmtsaure menthyl ester whose m.p. is 37°

1. C.C. 79, (1), p. 837.

2. Jr. Ch. Soc. 79, p. 1308.

3. Tschugaeff, ...........

Closely related to the benzoate are the phenyl-acetyl ester, phenyl-propionyl ester, ortho, meta, and para-toluyl esters of menthol, all prepared by Tschugaeff[1] in 1898 from the acid chloride and menthol.

1. Ber. Dtsch. Ch. Ges. 31, p. 360-68. & 1775-83.

## MENTHYL PHTHALATES.

Synonym; Ger. Phtalsauredimenthylester.

Fr. Orthophtalate de Menthyle.

History:- This ester was prepared by Arth[2] in 1886.

Preparation:-When theoretical amounts of phthalic acid and menthol are heated together at 135°-140° for 40 hours a solid forms which is the ester.

Properties:The melting point of the ester is 133°C, the specific rotation at 20° for the D line is -94°.72. This ester is soluble in alcohol but more so in ether.

## MENTHYL ACID PHTHALATE.

Synonym:- Ger. Phtalsauremonomenthylester.

Fr. Orthophtalate Acide de Menthyle.

History:- This ester was also prepared by Arth.[2]

Preparation:- By using one molecule of phthalic acid an-

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[1] Ber. Dtsch. Ch. Ges. 31, p. 360°-368° & 1775-82.

[2] Ann. Chim. (6), 7, p. 479.

hydride and one molecule of menthol and heating at 110°C for thirth six hoursthe ester was obtained.

Properties:- The ester is insoluble in water, soluble in alcohol, ether and chloroform. It has a rotation of -105°55 at a temperature of 20°. With KOH it forms the potassium salt.

## NAPHTHOIC ACID ESTERS OF MENTHOL.

Synonym:- Ger. Alpha-naphthoesäure Menthyl Ester.

These esters and their derivatives were prepared by Hans Rupe[1] for his work on optical rotation in which he used the acid chlorides and menthol.

## MISCELLANEOUS ESTERS OF MENTHOL.

There is still another class of saturated cyclic esters prepared by Rupe[1] in 1903 for his work on optical rotation. These, like all the rest, are prepared from menthol and acid chlorides. The following are the esters prepared by Rupe[1].

Menthyl ester of Trimethylenecarbonsäure
" " " Tetramethylenecarbonsäure
" " " Pentamethylenecarbonsäure
" " " Hexamethylenecarbonsäure

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[1] Yahresb. d. Forts. d. Ch. 56, (2), p. 797.

## MENTHYL ACETATE.

The method used for the preparation of menthyl acetate is the method given in the U.S.Pharmacopoeia*and in Gildermeister and Hoffmann* for the estimation of menthol in peppermint oils. This reaction is according to the equation:

$$2C_{10}H_{19}OH + (CH_3CO)_2O = 2C_{10}H_{19}OOCCH_3 + H_2O$$

Three separate quantities of 50c.c. of acetic acid anhydride, 5gms. of anhydrous sodium acetate and 25 gms. of menthol were heated in acetylization flasks over direct flames. The boiling continued calmly until after a certain time when the liquid boiled up violently and it continued to boil for five minutes after removal of the flame. No doubt this was the proper temperature at which the two substances combine to form the ester. After the mixture was cooled, it was washed with water, the excess acid neutralized with potassium carbonate, then washed again and dried over calcium chloride. The ester was then distilled under diminished pressure and the boiling point found to be 115° at 15m.m. pressure. On saponification with N/2 potassium hydroxide the following results were obtained which show the purity of the ester.

1. U.S.P. 1900, p.318

2.Die Aether ische Oele, p. 848

| Wt. of Ester | N/2 KOH used | % Ester |
|---|---|---|
| 2.8720 | 29.22c.c. | 100.05 |
| 2.7570 | 28.03c.c. | 99.98 |
| 2.7970 | 28.67c.c. | 100.70 |

The specific gravity at 20°C. was found to be .9230. The angle of rotation, which on Mar. 23, 1910 was found to be -72°.42, on May 7 had changed to -73°.14. On May 29,1911, the angle was found to be -72°.  .at 24°C. If any change in the composition did occur it was very slight and the difference in the above readings might be explained as an error in reading the angles. The index of refraction was found to be 1.4454

Comparing as far as possible the above results with those obtained by others, we find that the ester obtained by Bertram[1] has a boiling point of 109° at 10-11m.m. very near to the one given above; that of Tschugaeff[2] has a boiling point of 109° at 15m.m. pressure, 6 degrees lower than the one given above. Patterson & Taylor[3] give the boiling point at 22m.m. as 116°C. All other recorded boiling points are given at ordinary pressure and can therefore not be compared with those herein discussed.

There is a difference of only .002 between the specific gravity of the above ester and that obtained by

[1] Winther, Patente d. Org. Chem. Vol. 1, p. 623.

[2] Ber. d. Dtsch. Ch. Ges. 31, p. 364.

[3] Jr. Ch. Soc. Lon. 87, p. 33.

Kishner[1] a difference which may be due to the fact that Kishner compares the density at 20°C. to water at 0°. The density given by Tschugaeff[2] is rather low: $d\frac{20}{4}$ = .9185. That given by Berkenheim[3] is 0.9414 which is high; the density ( $d_{13}$= 0.9307) assigned by Patterson & Taylor[4] is about like that obtained in these experiments.

The specific rotation for the D line given by Kishner[1] (-79°.26) and Tschugaeff[2] (-79°.42) are high, whereas that obtained for the ester from the peppermint oil which is -72°.15 as given by Power & Kleber[5], is very nearly the same as obtained by the writer.

It is rather unsatisfactory to try to discuss the quality of the esters by comparing the physical properties alone, as these are influenced in various ways by outside causes. The saponification as given above in addition to the physical properties ought to be a better criterion of the purity of the ester obtained. An ester which will fill these requirements can therefore be used as a standard of comparison with greater satisfaction.

[1] Winther, Patente d. Org. Ch. Vol. 1, p. 623.

[2] Ber. d. Dtsch. Ch. Ges. 31, p. 364.

[3] C. 1893, 1, p. 982.

[4] Jr. Ch. Soc. Lon. 87, p. 33 .

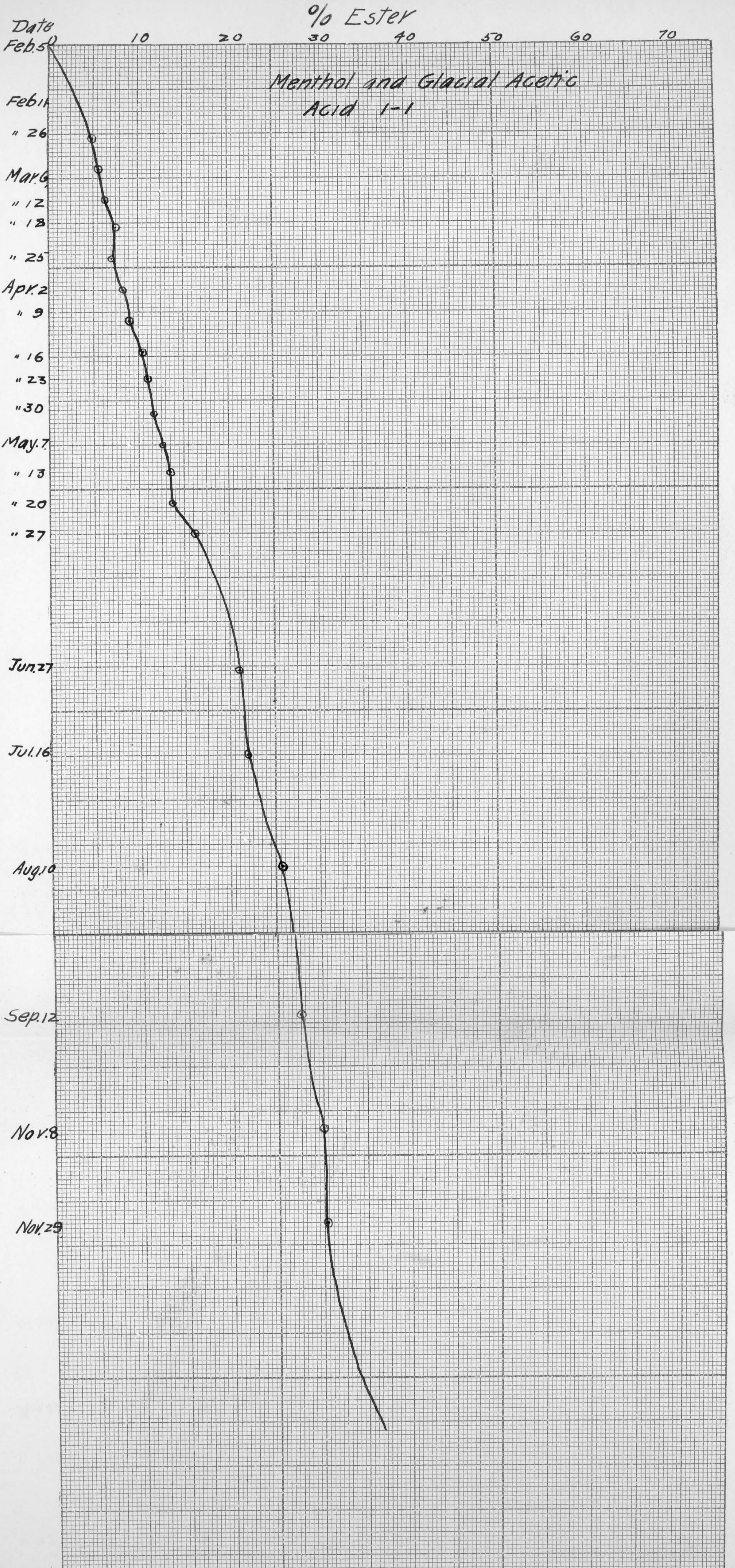
[5] Arch. d. Pharm. 232, p. 653.

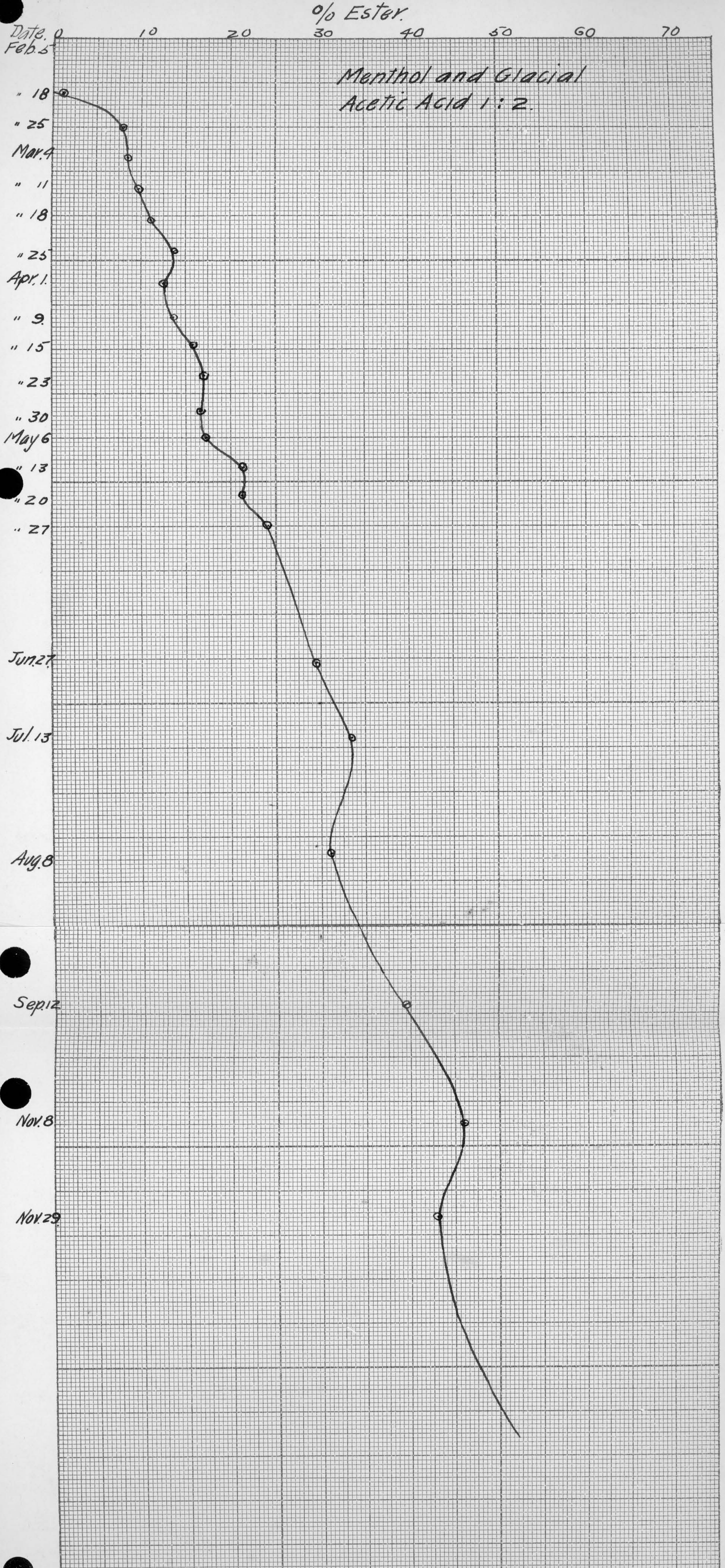
## SLOW ESTERIFICATION OF MENTHOL AND ACETIC ACID.

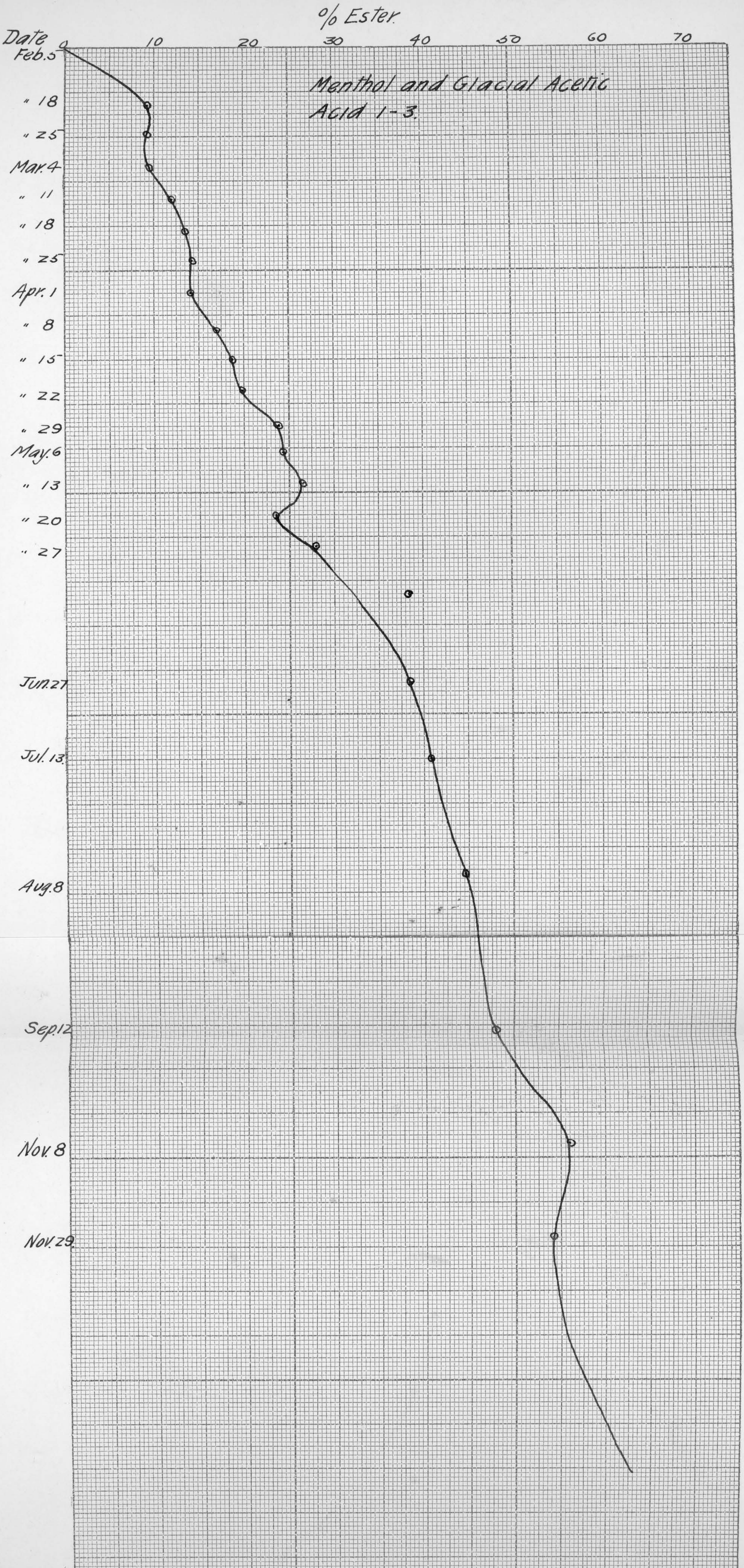
Both menthol and acetic acid occur in the oil of peppermint as does also the menthyl acetate. The study of the slow esterification which goes on when these two substances, menthol and acetic acid, are allowed to react with one another at ordinary temperature for a period of time, may help to explain the occurrence of the three named substances in the proportions found. Besides this, it is of some interest to note the rate of esterification with varying quantities of substances in contact.

Three ratios of the quantities of menthol to acetic acid were prepared on Feb. 4, 1910, at which time the specific gravity, rotation, and index of refraction were noted. These readings including saponification values were regularly taken at intervals of a week, covering a period of nine months. after which the readings were taken at longer intervals. After four months it was found that neither the density nor the index of refraction gave any information as to the ester formation. Unfortunately an error was made for the first few weeks in reading the rotation, but later the rotation and saponification showed a constant increase of ester content.

The following data was obtained from mixtures of 200 gms. of menthol and 88 gms. of glacial acetic acid, 200gms. of menthol to 176 gms. of glacial acetic acid and 200 gms. of menthol and 264 gms. of glacial acetic acid. In the first mixture the molecular proportions are 1:1,; in the second 1:2 and in the third 1:3. The ester content was always calculated for the percent menthol present in the mixture. In this way we could get a comparison of the amount of ester formed on the basis of equal amounts of menthol.


% Ester
Date
0
10
20
30
40
50
60
70
Menthol and Glacial Acetic
Acid 1-1
Feb.5
Feb.1
" 26
Mar.6
" 12
" 18
" 25
Apr.2
" 9
" 16
" 23
"30
May.7
" 13
" 20
" 27
Jun.27
Jul.16
Aug.10
Sep.12
Nov.8
Nov.29


Menthol and Glacial Acetic Acid 1:2.

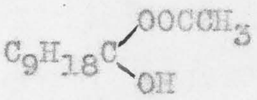

% Ester
Date
0
10
20
30
40
50
60
70
Menthol and Glacial Acetic Acid 1-3.
Feb. 5
" 18
" 25
Mar. 4
" 11
" 18
" 25
Apr. 1
" 8
" 15
" 22
" 29
May 6
" 13
" 20
" 27
Jun. 27
Jul. 13
Aug. 8
Sep. 12
Nov. 8
Nov. 29

From the data given the following conclusions may be drawn; that the greater the amount of acetic acid present the greater is the rate of esterification. In the peppermint oils this condition is usually reversed in that there is usually a large amount of menthol present which in some cases can be chilled out. Acetic acid however is generally present in only very small amounts. An excess therefore of either one of these substances means a corresponding small amount of the other with an ester content depending on the equilibrium between the two. From the periodic dips in the curves it might be concluded that changes in temperature may have a noticeable influence on the ester formation. The dips in the curves usually come at the same points for the three mixtures. The irregularity of the rate of ester formation is shown from the rotation values as well as the saponification values.

The data also shows that such properties as the specific gravity and the index of refraction are useless in determining the speed of reaction of this kind and that the saponification value and especially the rotation can be depended on:

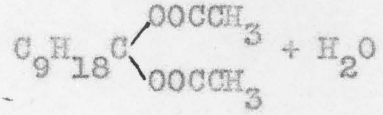
Similarly to the previous experiments on esterification, the slow action of menthone in contact with acetic acid over a long period of time was also studied. Only the saponification values and the angle of rotation were condidered, because, from the previous experiment it was found that the density and the index of refraction were useless in the determination of the rate of change of ester content.

As ketones have additive capacity and as alcohols form esters with acetic acid the following reaction was considered to go on. First one molecule of acetic acid is added on as shown:



$$C_9H_{18}C\begin{matrix}\diagup OOCCH_3 \\ \diagdown OH\end{matrix}$$

then a second molecule of the acid reacts, and by splitting off water a sort of di-ester of a glycoll results. The ester values are calculated on this basis.



$$C_9H_{18}C\begin{matrix}\diagup OOCCH_3 \\ \diagdown OOCCH_3\end{matrix} + H_2O$$

Such a combination of menthone and acetic acid has not been reported as occurring in plant products though the separate compounds do occur there.

For the following data 200 gms. menthone and 77.7 of glacial acetic acid, 150 gms of menthone to 116.55 gms. of glacial acetic acid and 100 gms. of menthone to 116.55

gms. of glacial acetic acid giving the molecular proportions as 1:1, 1:2, and 1:3.

## MENTHONE AND GLACIAL ACETIC ACID 1:1

| Date | Rotation | Date | % Ester |
|---|---|---|---|
| Jun.26, | +4° 24' 0" | Jun.26, | ..... |
| Jun.27, | + 4° 0' 0" | Jun.27, | 2.48 |
| Jul.15, | + 3°54' 0" | Jul.13, | 2.91 |
| Aug.10, | + 3°52'48" | Aug.10, | 3.34 |
| Sept.12, | + 4° 4'12" | Sep.12, | 3.13 |
| Nov.8, | + 3°57'36" | Nov.8, | 4.79 |
| Dec.1, | + 3° 7'48" | Dec.1, | 4.73 |
| May.15, | + 3° 0'21" | May.13, | 7.39 |

## MENTHONE AND GLACIAL ACETIC ACID 1:2

| Date | Rotation | Date | % Ester |
|---|---|---|---|
| Jun.26, | - 2°38'24" | Jun.26, | ..... |
| Jun.27, | - 1°48' 0" | Jun.27, | 2.56 |
| Jul.15, | - 0°44'24" | Jul.13, | 5.11 |
| Aug.10, | - 0°17'24" | Aug.10, | 2.46 |
| Sep.12, | + 1° 3'36" | Sep.12, | 3.13 |
| Nov.8, | + 1°22'36" | Nov.8, | 4.39 |
| Dec.1, | + 2° 1'48" | Dec.1, | 5.38 |
| May.15, | + 1°54' 0" | May.13, | 7.18 |

## MENTHONE AND GLACIAL ACETIC ACID 1:3

| Date | Rotation | Date | % Ester |
|---|---|---|---|
| Jun.26, | - 6°53'24" | Jun.26, | ..... |
| Jun.27, | - 4°45' 0" | Jun.27, | 5.05 |
| Jul.15, | - 2°56'24" | Jul.13, | 2.86 |
| Aug.10, | - 1°25'12" | Aug.10, | 3.54 |
| Sep.12, | - 0° 1'48" | Sep.12, | 3.26 |
| Nov.8, | + 0°41'24" | Nov.8, | 5.28 |
| Dec.1, | + 1°12' 0" | Dec.1, | 8.45 |
| May.15, | + 2°47'24" | May.13, | 11.01 |

Like the preceding experiments on esterification, the rate of esterification between menthone and acetic acid increased with the amount of acetic acid present. The rate of esterification is irregular as shown by the saponification and rotation values due no doubt to external influences. From the data it is seen that the ester formed very slowly. It was therefore supposed that an equilibrium had set in so that as soon as the ester had formed it was again partially hydrolized. To establish this fact, part of the acetic acid was replaced by such an amount of acetic anhydride which, with the water formed through esterification would form acetic acid which, with the original amount would make the proportion of menthone to acetic acid 1:2. For this purpose 71 gms. of menthone, 27.7 gms. of glacial acetic acid, and 23.5 gms. of acetic anhydride were used. The rotation of this mixture was +6° 43' 12". In six months the rotation had increased to +7° 21' and the amount of ester was 31.78%. From the tables a similar mixture of 1 part of menthone to 2 parts of acetic acid ( molecular weights.) gave after about a year only 7.18% ester. This shows conclusively that the supposition was correct.

## MENTHYL BENZOATE.

The most simple method of preparation of menthyl benzoate which suggested itself is that of bringing together menthol and benzoyl chloride. These substances in molecular proportions according to the reaction

$$C_{10}H_{19}OH + C_6H_5COCl = C_{10}H_{19}OOCC_6H_5 + HCl$$

were heated to boiling in a flask with a reflux condenser. The mixture boiled at 145°C. outside temperature. During the heating fumes of HCl escaped which were identified by holding a moistened piece of filter paper near them and also by the odor. After all ebullition at this temperature had ceased, the mixture was distilled under a 15 m.m. vacuum up to a temperature of 145°C. at which everything but the benzoate was expected to have distilled over. The melting point of the crude ester formed was between 47°-55°C. Ten gms. of this ester were next thoroughly shaken with cold alcohol when 5.3 gms. remained undissolved which had a melting point between 37°-56°C. the greater amount melting near the lower temperature showing the presence of free menthol.

The crystals obtained from the solution of menthyl benzoate had a melting point of 49°-56°C. most of the ester melting at about 53°C. When recrystallized from alcohol, the crystals melted between 54° and 56°C. and a crusty substance remained which invariably melted lower.

After several attempts to obtain the ester pure by the above method of crystallization, it was found that the mixture of menthol and the menthyl benzoate when crystallized from benzene, gave a greater yield of crystals melting between 54° and 56°. This showed that the alcohol had some action on the crystallization of the ester. An analysis was attempted of the original mixture as it comes from the flask after distillation. Acetic anhydride was added to acetylize the supposed excess of menthol and the mixture heated. No satisfactory results were obtained on saponification. It was later found that the saponification of the ester could not be depended on.

The above method was dropped because of its inefficiency and the benzoic acid anhydride method taken up. The preparation of the anhydride offered the first difficulty. Three methods for the preparation of this anhydride were attempted.. The first was the following method given by Autenrieth.[1]: Benzoic acid and acetic acid anhydride in the proportion of 1 to 3 were allowed to stand in contact for several hours, after which the mixture was heated for several more hours to boiling.with the use of a reflux condenser. From the mixture the excess of acetic acid and acetic anhydride were distilled and the remaining substance in the flask washed with soda solution and then extracted

[1] Ber. d. Dtsch. Ch. Ges. 34, p. 184.

with ether. On evaporation of the ether a mixture of benzoic acid anhydride and acetic-benzoic acids anhydride are obtained. To free the benzoic acid anhydride from the acetic-benzoic acid anhydride, the mixture was boiled with a 5% soda solution; this was kept up with thorough shaking until a sample taken out and dropped into ice water immediately solidified. Too much heating should be avoided as sodium benzoate is likely to form. The anhydride was then dissolved in 50% acohol after being washed with water and then precipitated with a large amount of water. On cooling benzoic acid anhydride was obtained which had a fruity odor and which ought to have had a melting point of 42°C. Everything seemed to work satisfactorily according to these directions but when the melting point was tried it gave values near that of benzoic acid. No doubt the anhydride was hydrolized in some way because the exact conditions were not obtained. This method was so long and questionable in its results that others were tried instead.

The second method for the preparation of the anhydride was suggested by Ch. Gerhardt[1] who made use of the double decomposition between sodium benzoate and benzoyl chloride as follows:

$$C_6H_5COONa + C_6H_5COCl = (C_6H_5CO)_2O + NaCl$$

Dry sodium benzoate was mixed in molecular proportions

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[1] Ann. 87, p.73.

with benzoyl chloride and heated on a sand bath to 130°C. A clear solution resulted and when the temperature was incresed sodium chloride separated out. After the mass was cooled it was washed with cold water and then with soda solution. The residue is benzoic acid anhydride. This was crystallized from hot alcohol. On cooling the anhydride is supposed to separate out as an oil which will then crystallize. Too much alcohol should be avoided since the anhydride is lost in the formation of ester. When the melting point of this material obtained was determined, it was found to melt at about the temperature. of benzoic acid and also had that crystalline appearance. This method was also abandoned.

A third method of heating together neutral pottasium oxalate and benzoyl chloride according to the reaction:

$$2C_6H_5COCl + (COOK)_2 = (C_6H_5CO)_2O + 2KCl + CO + CO_2$$

was next tried, a method also worked out by Gerhardt[1]. His directions are as follows: " Pottasium oxalate is heated to free it from water of crystallization and then powdered. Equal quantities of this salt and the benzoyl chloride are heated together with constant shaking. The reaction is complete when no odor of benzoyl chloride remains." The anhydride is further purified by the same method as in the

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1. Ann. 87, p.73.

preceding experiments. No better results than before were obtained.

A method found very satisfactory is that suggested by Anschuetz[1z] who heated oxalic acid with benzoyl chloride.

$$(COOH)_2 + 2C_6H_5COCl = (C_6H_5CO) \quad + 2HCl + CO_2 + CO$$

In this case all of the side products are gases and can be easily expelled. The oxalic acid was first dehydrated in an air bath up to 110°C. then pulverized, placed in a vacuum of 30 m.m. and heated externally up to 120°C. An excess of benzoyl chloride was added to this dehydated oxalic acid and the two heated externally to 140°-150°C. when a strong action took place. The gases formed were allowed to escape. The heating was continued until no more HCl or carbon dioxide was given off. The excess of benzoyl chloride was then distilled off up to 175°C. at 35 m.m. pressure. At this temperature no benzoic acid anhydride came over. The anhydride was extracted with ether, this mixture washed with water and then washed with dilute ammonia to get rid of remaining benzoyl chloride. The ether was evaporated off and the benzoic acid anhydride heated with petroleum ether to effect solution. No anhydride seemed to dissolve but in the molten condition it formed the lower layer from which it crystallized leaving the supernatent liquid of a

[illegible]

1. Ann. [illegible]

brownish color due no doubt to the impurities from the anhydride. After the crystals were washed with petroleum ether they melted at 42°C. and had a sweet fruit odor.

In the preparation of the menthyl benzoate, twice the molecular proportion of anhydride to the menthol according to the reaction,

$$(C_6H_5CO)_2O + C_{10}H_{19}OH = C_{10}H_{19}OOCC_6H_5 + C_6H_5COOH$$

were placed in a sealed pop bottle buried under sand and heated at a temperature of 180°C. for 1 3/4 hours. When the bottle was opened no odor of menthol remained; this shows the complete conversion into the ester. This mixture was then transferred to a distilling flask and everything distilled off up to 180°C. at 40 m.m. a temperature somewhat lower than the boiling point of the menthyl benzoate which is 180° at 15 m.m. pressure. The remaining mass was extracted with ether, this mixture washed with dilute sodium hydroxide to remove remaining benzoic acid; then, with water and the ether finally evaporated. When crystallized from petroleum ether, large prismatic white crystals resulted which had a melting point of 55.5°C. The rotation of a two per cent solution of these crystals in alcohol for a 100 m.m. tube, D line at a temperature of 24°C. was 1°.81 which gives a specific rotation of -90°.5.

COMPARISON: No other record shows such a high melting point for this ester. This seems to be the correct melting point of the above ester as after several recrystallizations in the same manner the ester still had this melting point. The rotation is lower than that obtained by others. Since the other investigators do not give the temperature at which the rotation was taken, a satisfactory comparison can not be made. If this difference is to be accounted for, it may be due to the concentration of the solution or to the inherent difference of the ester.

## MENTHYL STEARATE.

An attempt was made to prepare menthyl stearate from menthol and stearic acid anhydride as suggested by Beckmann[1]. For the preparation of the stearic acid anhydride, 40 gms. of stearic acid were heated with 25 gms. of acetic anhydride in a sealed bottle up to 160° for six hours. The mixture was washed with water, then with dilute sodium acid carbonate and dried between porous plates. Before washing with the 5% soda solution, the stearic acid anhydride had a melting point of 47°-55.5°C.; after washing the melting point was close to 55°C.

Molecular proportions of the anhydride and menthol were boiled at a temperature of 180°C. for three hours. No special action took place except that when the liquid which condensed in the reflux condenser dropped back to the mixture it caused a crackling noise in the flask and the liquid boiled up more violently. On cooling, a yellow mass formed which was extracted with alcohol, and the alcohol evaporated. The supposed ester gave a melting point of over 72°C. about the melting point of stearic acid.

Because this method did not give very satisfactory results the Beckmann[1] method was tried. 50 gms. of stearic acid and 8.2 gms. of sodium hydroxide were boiled together and then evaporated to dryness. To the sodium

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[1] Jr. f. Pr. Ch. 55, (2), p. 14-31.

stearate suspended in benzol phosphorus oxy-chloride was added. Two layers formed, the lower probably water and dissolved salt; the upper of which was the anhydride in the benzol which was evaporated when a liquid remained which solidified into a brownish white mass and whose melting point was 47°-57°C.

When this anhydride was heated with the molecular amount of menthol at 180°C. for 3 hours, a white powder of strong menthol odor was obtained whose melting point was between 55°-65°C. and which when rubbed between the fingers felt smooth and melted.

Both products from the above experiments had rather low melting points and it was thought that these mixtures might contain ester in part. The separation of this ester offered a great difficulty. If excess menthol were present, this could be distilled off under vacuum. If the ester had a high boiling point and were not decomposed at a high temperature the stearic acid could also be distilled off. This was tried but after the menthol came off, the remaining liquid turned brown which was a sign of decomposition.

Another method of heating together stearyl chlor- and menthol suggested itself. The stearyl chloride was prepared by grinding together in a mortar, stearic acid and phosphorus penta-chloride and heating the two slightly on a water bath. The excess of phosphorus pentachloride was distilled off. The stearyl chloride was heated with menthol to 150°C. for one hour. The resulting liquid when allowed to cool, crystallized. This mass was distilled una vacuum of 40 m.m. when menthol came over at 103°C. A liquid, probably stearyl chloride also came over. The residue solidified and no longer had any odor of menthol. This residue was dried between porous plates and when pressed between the fingers melted. On saponification, the stearate content was found to be 114% and 115.1%. which showed that an excess of stearic acid was present.

The experiment was repeated but the resulting residue after distillation again turned brown and had a melting point of 58.5°C. The saponification value was too far off to be considered. From the above experiments it was concluded that the brown mass which formed contained only the ester and stearic acid as the menthol could be distilled off. To remove the stearic acid seemed to be the only way to obtain a pure ester. An alkali as sodium or pottasium hydroxides was thought would be likely to break up the ester. Hydrated barium oxide was therefore used to precipitate the stearic acid. The mixture of stearic acid and ester in powder form with water was shaken with bariumoxide. The mass was then shaken with ether which was to extract only the ester and leave the salt of the acid. When the ether was evaporated, a residue was left which had a crystalline appearance and which had a melting point of about 75°C. very near to that of stearic acid.

Calcium chloride in alcohol was next shaken with an alcoholic solution of the ester stearic acid mixture to form an insoluble salt of stearic acid. This also failed to produce the pure ester. Later work on the preparation of sodium stearate showed with what difficulty an alkali combined with free stearic acid. This no doubt explains why no insoluble salt of stearic acid had formed and why the melting point of stearic acid was always obtained.

The only way which seemed to offer any possibility of obtaining a pure ester was that of double decomposition between menthyl chloride and silver stearate or some other stearate. Menthyl chloride was prepared by the common method of halide formation from alcohols treatment with phosphorus pentachloride. Berkenheim[1] used the method of covering the phosphorus pentachloride with petroleum ether, pouring into this a cold solution of menthol in petroleum ether and keeping the whole with ice. As time of reaction and rise in temperature change the products, everything was done speedily and at a low temperature. The redulting solution in petroleum ether was thoroughly washed with ice water and the ether layer separated from which the petroleum ether was evaporated. Both the dextro and laevo menthyl chlorides are formed by this

[1] Ber. d. Dtsch. Ch. Ges. 25, p. 686.

means. To get rid of one of these chlorides, Kursanow[1] suggests treating the mixture with alcoholic potassium hyddroxidewhen only the dextro menthyl chloride breaks up into menthene and potassium chloride and leaves the laevo menthyl chloride. When treated in this way the solution became very hot and potassium chloride formed; two layers appeared after distilling off the alcohol. These were separated and the heavier one fractionated. From the preparation of five separate quantities the following results were obtained.

| | B. P. | Press. m.m. | Sp.Gr. (20°) | Rotation (20°) | Index. of Ref (20°) |
|---|---|---|---|---|---|
| 1. | 111° | 33 | .9140 | -7.16° | 1.4588 |
| 2. | 120° | 62 | .9150 | -5.68° | 1.4565 |
| 3. | 120° | 52 | .9125 | -6.07° | 1.4560 |
| 4. | 120° | 52 | .9252 | -6°.5 ° | 1.4587 |
| 5. | 115° | 34 | .9293 | -6.45° | 1.4593 |

All of these products were mixed, fractionated, and refractionated. The boiling point at 30 m.m. was then found to be 111°; the rotation at 20°, -6.48°; specific gravity at 20°, .9194; and index of refraction, 1.4587.

When part of this menthyl chloride was heated with alcoholic potassium hydroxide, potassium chloride was produced which dissolved in water and precipitated sil-

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[1] C. 72, (2), p. 347.

ver chloride on addition of silver nitrate. The liquid was then fractionated, when the remaining menthyl chloride boiled at 115° at 34 m.m. pressure.and had a rotation of -7.18°. These results differ widely from those of Kursanow[1] who gives the boiling point at 13.5 m.m. as 113.5°- to 114°, the density at 20° as .9411, and the specific rotationas -50.56°. The resulting halide was a clear liquid with a characteristic halide odor. It was insoluble in water but soluble in alcohol, ether, chloroform, benzene and petroleum ether, also in heptane. When distilled it decomposed and had a green tint which could be got rid of with mercury.

Sodium stearate was the first salt of stearic acid prepared. The stearic acid was dissolved was dissolved in absolute ether,and when metallic sodium was added a white precipitate formed. This, it was decided, was the anhydrous sodium stearate. In the form of powder, however, it would not dissolve in water. Analysis showed that it contained less than 50% of sodium stearate. This substance could therefore not be used.

To prepare silver stearate it was necessary to have sodium stearate. A 2N solution of sodium hydroxide to avoid presence of sodium carbonate, was heated with the molecular quantity of stearic acid for six hours and

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[1] C. 72, (2) 347.

and at a slight pressure. The mass formed would not dissolve in water. A similar mixture was then heated for about 30 hours. While this was still in a molten condition it was poured into water and dissolved quite readily. To this solution was added a solution of silver nitrate, and a voluminous cheesy precipitate came down. This was washed until no precipitate with hydrochloric acid was obtained in the wash water, and dried on a porous plate. The mass turned slightly grayish blue. Analysis showed less than 50% silver stearate. Further investigation of this matter showed that according to Lewkovitch, on dilutioh sodium stearate forms a sodium acid stearate.

$$C_{17}H_{35}COONa.C_{17}H_{35}COOH$$

If we consider that the supposed silver stearate is a silver sodium stearate similar to the above, the actual amount of silver stearate will be close to 73%.

Another sample of the mixture was shaken with acetone and thoroughly washed with acetone to dissolve out the sodium stearate. This was followed with ether and then alcohol. The silver stearate was dried on a porous plate. On analysis it gave the following results;

Wt. of silver stearate= .3517gms.
Wt. of Silver. = .1013
% silver stearate = 105.2

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these results show that the stearate of silver can be purified in this way. The per cent is too high and is due to the drying on the porous plate as some of the dust of the plate became mixed with it.

Silver stearate which for the above reason analized to 104.3% pure, was mixed in molecular proportions with purified menthyl chloride and heptane added to bring about contact. This mixture was heated in a sealed bottle at a temperature between 150° and 165°C. for three hours when the stopper gave way and the products were lost. A brown smeary substance remained in the bottle and after a few days seemed to form feathery crystals.

In all of the experiments on the menthyl stearate no melting point was obtained as low as that given by Beckmann[1] which is 39°. It was thought possible that Beckmann obtained only the melting point of a eutectic mixture of menthol and stearic acid. To discover whether or not this supposition was true, the writer determined the melting point of a mixture of menthol and stearic acid in molecular proportions, and found it to be 49° The melting points of the substances obtained in the above experiments were close to 49° . From this fact it may be concluded that these substances may have been eutectic mixtures.

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[1] Jr. f. Pr. Ch. 55, (2) p. 14-31.