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SYNTHESES IN THE NAPHTHALENE SERIES.

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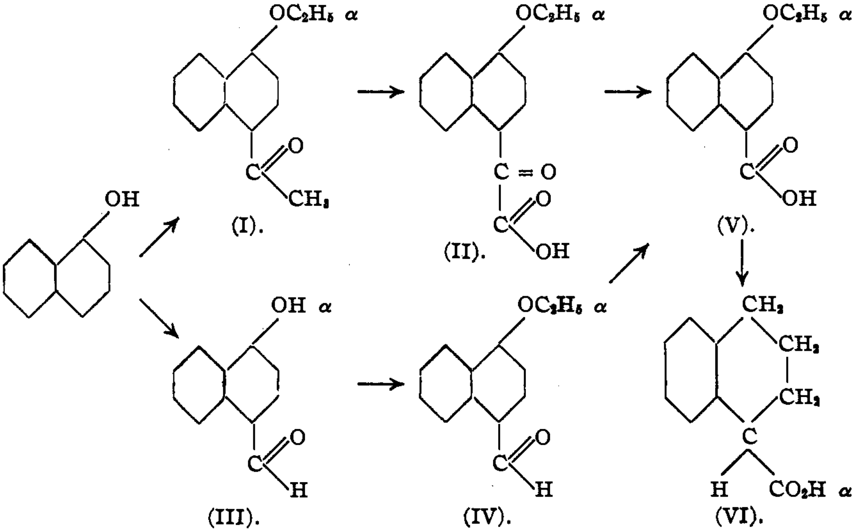
The primary object of this research has been the preparation and proof of the atomic linking structure of 1,4-ethoxynaphthoic acid.

In the course of an investigation concerning the action of amidoformyl chloride on the ethers of α-naphthol, Gattermann[1] prepared an ethoxynaphthoic acid which was assumed by analogy to be the 1,4-isomer. In the present work, a more convenient method of preparation was sought and preferably one which would serve for an absolute demonstration of structure. Additional independent evidence for the structures of all of the intermediate products in this synthesis has been obtained incidentally. The individual steps in the synthesis are illustrated by the following formulas:



α-Ethoxyacetonaphthalene (I) was prepared from the ethyl ether of α-naphthol by means of the Friedel and Crafts reaction, and from this ketone, by oxidation, α-ethoxynaphthoyl formic acid (II) and α-ethoxynaphthoic acid (V) were prepared. It may, therefore, be stated that the ethoxy group in Formula V is in the alpha position, since the compound was prepared from α-naphthol. If we were to reason by analogy to other well-known reactions, the carboxyl group would be expected to lie in the para position with respect to the ethoxy group but in order to make no assumptions whatsoever, we will state that we are here dealing with one of the seven possible α-ethoxynaphthoic acids.

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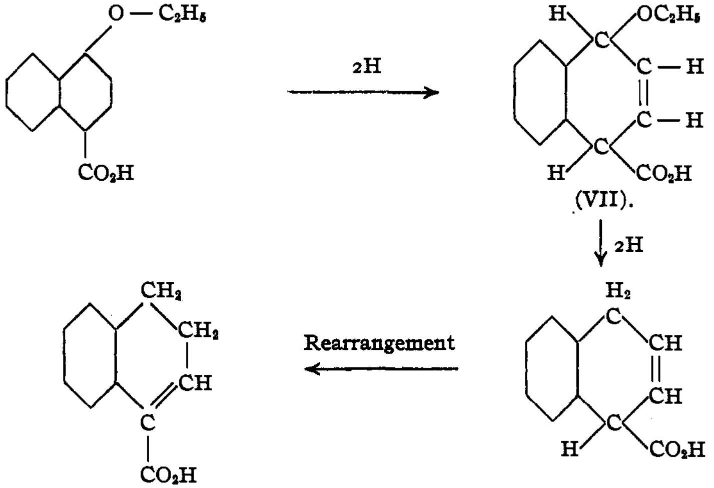
[1] *Ann.*, 244, 73 (1888).

The same ethoxynaphthoic acid was synthesized, however, according to a second method. α-Naphthol aldehyde[1] was prepared from α-naphthol and from the former α-ethoxynaphthol aldehyde (IV) was obtained. The oxidation of the latter yielded the same α-ethoxynaphthoic acid as that prepared from α-ethoxyacetonaphthalene. Since, however, α-naphthol aldehyde was easily oxidized to phthalic acid, we know that the two substituents are in the same ring. Therefore, in the ethoxynaphthoic acid (V), the two substituents are in the same ring[2] and at least one substituent is in the alpha position. The seven possibilities are thus reduced to but three.

When α-ethoxynaphthoic acid (V) was reduced with sodium amalgam, the ethoxy group was eliminated and tetrahydro-α-naphthoic acid obtained. The latter was identified not merely by its melting point and analysis but also by its ionization constant which is almost 100% greater than that of tetrahydro-β-naphthoic acid. It is therefore demonstrated that the carboxyl group in α-ethoxynaphthoic acid is also in the alpha position, and, since both groups are in the alpha positions and also in the same ring, they must be in the 1,4-positions. These facts demonstrate completely the structure of 1,4-ethoxynaphthoic acid and at the same time demonstrate the structures of all the intermediate products from which this acid was prepared.



(VII).

(IX). (VIII).

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[1] We wish to thank Professor J. B. Ekeley, of the University of Colorado, who has given us a sample of Schuchardt's α-naphthol aldehyde for comparison with our product.

[2] Additional evidence for this statement is found in the recent work of Witt and Braun (*Ber.*, 47, 3228). α-Ethoxyacetonaphthalene may be dealkylated and the resulting naphthol may be oxidized to phthalic acid.

We have recently repeated the reduction of 1,4-ethoxynaphthoic acid and have subjected it to a less vigorous reduction than before in order to prevent the elimination of the ethoxy group.

By analogy to the behavior of α-naphthoic acid under similar conditions, the dihydro-ethoxynaphthoic acid represented by Formula VII would be expected as the first reduction product. We have not been able to isolate this product, but have obtained instead Δ^2-dihydronaphthoic acid-1 (VIII) from which, by rearrangement, the Δ^1-acid (IX) was prepared. This substantiates completely the conclusions drawn in the preceding paragraph in regard to the position of the carboxyl group in the ethoxynaphthoic acid.

Gattermann, Ehrhardt and Maisch[1] have prepared α-ethoxyacetonaphthalene (I) while making a study of the Friedel and Crafts synthesis of ketones. They state that the two groups are probably in the para positions but this fact was not proven. Recently, however, Witt and Braun[2] have given more definite evidence for the structure of this compound and the independent proof given in our work has substantiated this evidence.

A compound believed to possess the structure of the keto acid (Formula II) was synthesized by Rousset[3] by the action of ethyl oxalic acid chloride upon α-ethoxynaphthalene, followed by the subsequent hydrolysis of the ester. We find that our product agrees in its properties with this keto acid and its structure is therefore demonstrated beyond the possibility of a doubt. The previous assignment of structure based upon the structure of 1,4-ethoxynaphthoic acid[4] was open to the objection that the structure of the latter product had not been demonstrated.

α-Ethoxynaphthyl aldehyde was prepared by Rousset[5] by an independent method and was found to be identical with our product (IV) from which 1,4-ethoxynaphthoic acid was prepared. Its structure as a 1,4-derivative, as well as the structures of all derivatives prepared from it, is confirmed.

1,4-Ethoxynaphthoic acid was found to be identical with the acid prepared by Gattermann and Hefs[6] by an independent method. The structure of Gattermann's acid is therefore definitely assigned. Finally, it may be pointed out that the syntheses described above present final evidence in favor of structure (III) for the naphthol aldehyde prepared by Gattermann and Horlacher.[7]

[1] *Ber.*, **23**, 1209 (1890).

[2] *Ibid.*, **47**, 3216 (1914).

[3] *Bull. soc. chim.*, [3] **17**, 811 (1897).

[4] *Ann.*, **244**, 74–75 (1888).

[5] *Loc. cit.*

[6] *Ann.*, **244**, 73 (1888).

[7] *Ber.*, **32**, 284 (1899).

Experimental Part.

Ethyl Ether of α-Naphthol.—This product was easily prepared by the action of diethyl sulfate upon an aqueous solution of the sodium salt of α-naphthol according to the usual procedure. From 50 g. of α-naphthol and 54 g. of diethyl sulfate a yield of 51 g. of the ether (85%) was obtained. Because of the relatively high cost of diethyl sulfate, the method of preparation recommended by Witt and Schneider[1] was found to be more economical. A mixture of 72 g. naphthol, 85 cc. potassium hydroxide solution (36%), and 90 g. potassium ethyl sulfate was placed in a bomb tube[2] and heated to 150° for six hours. The reaction mixture was treated with water and extracted with ether. In order to insure a product free from naphthol, the ether extract was shaken repeatedly with dilute alkali. The product was colorless and boiled at 280° under atmospheric pressure, at 186–187° under 66 mm., and at 152–154°, when the pressure was reduced to 18 mm. The yield was 66% of the theoretical. All unchanged α-naphthol, however, was recovered.

α-Ethoxyacetonaphthalene.—This compound was prepared by the Friedel and Crafts reaction according to the procedure given by Gattermann, Ehrhardt, and Maisch.[3] The purest product was obtained when the ether and the aluminum chloride were combined in exactly molecular proportions. An excess of the chloride produces a highly colored product and an increased amount of impurities. For this same reason, excessive heating of the reaction mixture must be avoided.

One mol. of α-ethoxynaphthalene was dissolved in two volumes of dry carbon disulfide and 1.5 mols. of acetyl chloride added. To this mixture, one mol. of fused powdered aluminum chloride was added in portions. After the evolution of hydrochloric acid gas was nearly complete, the reaction mixture was warmed to a temperature of 40° for about 15 minutes. The product was isolated as directed in the reference cited above. The yield was about 60% of the theoretical and the melting point of the product was 77°, as previously reported. The ketone may be purified best by distillation under diminished pressure. The boiling point was found to be 254–256° at 66 mm. pressure, the temperature of the outside bath being 292–294°. The product was found to be only slightly volatile with water vapor, but in order to examine its homogeneity we have subjected a one-gram portion to steam distillation, and collected it in fractions. The material purified in this manner was pure white, and no fraction varied from the melting point of the original material. This demonstrated that purification in addition to distillation is unnecessary.

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[1] *Ber.*, 34, 3171 (1901).

[2] A piece of galvanized iron pipe two inches in diameter, six inches in length, and closed at each end by threaded caps, was found very convenient for this purpose.

[3] *Ber.*, 23, 1199 (1890).

Oxidation of α-Ethoxyacetonaphthalene to α-Ethoxynaphthoyl Formic Acid.—The ketone was oxidized by alkaline permanganate. Ten grams of the product were added to 200 cc. of water containing 1 g. of sodium hydroxide and the mixture heated to boiling under a reflux condenser. A mixture of 17 g. potassium permanganate dissolved in 250 cc. of hot water was then added gradually. The permanganate color disappeared rapidly. Finally, the mixture was cooled and filtered from the manganese dioxide and from any unchanged ketone, and the free keto acid obtained by acidification of the alkaline solution. The yield was about 50% but a considerable amount of unchanged ketone was recovered from the manganese dioxide by dissolving the latter in a sulfite solution. The yield of acid based upon the amount of ketone actually oxidized was about 75%.

The crude product melted at 152–154° and possessed a lemon color. It was purified by recrystallization from dilute acetic acid and finally from alcohol. It may also be recrystallized from benzene. Its melting point after purification was 162°.

Subst., 0.1037 g.; CO_2, 0.2634 g.; H_2O, 0.0482 g.; Theory: C, 68.85%; H, 4.93%; Found: C, 69.23%; H, 5.16%.

Subst., 0.2203 g., 7.21 cc. alkali (0.113 *N*); Subst., 0.1500 g., 5.41 cc. alkali (0.113 *N*); neutral equivalent: Theory: 244. Found: 246, 245.

1,4-Ethoxynaphthoic Acid. (*a*) Preparation from α-Ethoxynaphthoyl Formic Acid.—An excess of potassium permanganate does not oxidize the keto acid to the corresponding ethoxynaphthoic acid. When, however, the oxidation is carried on in acid solution, this oxidation takes place very smoothly.

The keto acid was dissolved in hot 50% acetic acid solution using barely enough solvent to dissolve the product. To this solution there was added under the reflux condenser a hot 50% acetic acid solution of 5% more than the calculated amount of potassium permanganate to oxidize the glyoxalic acid group to a carboxyl group and carbon dioxide. The oxidation took place readily and it was necessary to add the oxidizing agent gradually in order to prevent too vigorous an ebullition due to the escape of carbon dioxide. Since the ethoxynaphthoic acid is less soluble than the original ketonic acid, it will partly crystallize out from the solution during the oxidation.

The acetic acid mixture was poured into water and the insoluble acid filtered off. Since it possessed a light brown color due to the presence of a small amount of manganese dioxide, it was dissolved in very dilute alkali and reprecipitated after filtration of the alkaline solution. Even the crude product thus obtained was practically pure, since it was almost colorless and melted at 217°. It was recrystallized from 95% alcohol (from which it crystallized in small needles) but its melting point remained unchanged. The yield was nearly quantitative.

(*b*) **Preparation from 1,4-Ethoxynaphthyl Aldehyde.**—The aldehyde, prepared according to the procedure given in the following section, was oxidized with alkaline permanganate. The acid obtained melted at 215–216° and was found to be identical with the acid prepared from α-ethoxynaphthoyl formic acid. A mixture of the products prepared by the two methods was found to melt at 216°.

1,4-Ethoxynaphthoic acid is very sparingly soluble in water. α-Naphthoic acid is soluble in water only to the extent of one part in 10,000. The introduction of the ethoxy group into the para position decreases the solubility at 25° to about one part in 60,000. Its solubility in hot water (90–100°) is also almost negligible; it was found to be one part in 22,000.

Gattermann has reported that the α-ethoxynaphthoic acid prepared by him forms a sodium salt which is only sparingly soluble in water. This agrees also with our observations on 1,4-ethoxynaphthoic acid.

Preparation of 1,4-Naphthol Aldehyde.—This product was prepared according to the directions given by Gattermann and Horlacher.[1] As a convenient method of purification, fractional precipitation from a methyl alcohol solution by the addition of water, is recommended. In this manner an almost colorless product was obtained. Its acetyl derivative melted at 110°.

Subst., 0.1525 g.; CO_2, 0.4078 g.; H_2O, 0.0630 g. Theory for $C_{13}H_{10}O_3$: C, 72.9%; H, 4.71%. Found: C, 72.9%; H, 4.58%.

1,4-Ethoxynaphthol Aldehyde.—Five g. of naphthol aldehyd were dissolved in dilute potassium hydroxide solution, 12 g. of diethyl sulfate added, and the mixture heated under the reflux for about one-half hour. The ether aldehyde which separated on the surface of the liquid was taken up with ether. The ether layer was shaken with alkali, dried, and evaporated. The brown-colored product remaining was recrystallized from dilute acetic acid, when an almost white product, melting at 72° was obtained. This melting point agrees with that given by Rousset.[1] The structure of this product is demonstrated by its oxidation to 1,4-ethoxynaphthoic acid.

Reduction of 1,4-Ethoxynaphthoic Acid to Ac-tetrahydro-α-naphthoic Acid.—Five grams of ethoxynaphthoic acid were reduced in a hot alkaline solution with 3% of sodium amalgam. A stream of carbon dioxide was passed into the solution in order to neutralize most of the alkali liberated. The first 200 g. portion of amalgam reacted readily, thus indicating that reduction was taking place, and this fact was confirmed by the permanganate test. The ethoxy acid does not readily reduce an alkaline permanganate solution and this is true also of tetrahydro-α-naphthoic acid. The intermediate reduction products, however, react in the typical manner of the ethylene compounds and for this reason the progress of the reduction

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[1] *Loc. cit.*

may easily be followed. After 1200 g. of amalgam had been used, reduction was found to be complete. The acid recovered from the alkaline solution melted at 81°, a value slightly lower than that of pure tetrahydro-α-naphthoic acid.[1] A determination of its neutral equivalent indicated that the ethoxy group had been eliminated in the reduction.

I. 0.1390 g. acid, 9.35 cc. KOH solution (0.0850 *N*). II. 0.0916 g. acid, 6.20 cc. KOH solution (0.0850 *N*). Neutral equivalent found: (1), 175; (2), 174. Theory for $C_{10}H_{11}CO_2H$: 176.

The melting point is not sufficient to differentiate between the two possible tetrahydronaphthoic acids, alpha and beta. For this reason we have compared the ionization constant of this product with that of the two tetrahydro acids obtained from α- and β-naphthoic acids,[2] respectively, *viz.*,

$$K_a^{25°} \text{ ac-tetrahydronaphthoic acid-1} = 4.43 \times 10^{-5}.$$
$$K_a^{25°} \text{ ac-tetrahydronaphthoic acid-2} = 2.47 \times 10^{-5}.$$

The value actually found was 4.2×10^{-5}, which agrees well enough with the former value to show that the carboxyl group of α-ethoxynaphthoic acid is in the α position. However, additional evidence is presented in the following section.

Intermediate Products in the Reduction of 1,4-Ethoxynaphthoic Acid to Tetrahydro-α-naphthoic Acid.—The reduction described in the preceding section was repeated except that the reaction was carried on at room temperature and a smaller proportion of sodium amalgam was used (150 g. 3% amalgam for 5 g. of the acid). The acids isolated from the reduction mixture were purified by fractional precipitation, but it was found that the only product present in addition to unchanged α-ethoxynaphthoic acid was Δ^2-dihydro-α-naphthoic acid (m. p. 85°). Since this acid is appreciably soluble in water (1 part in 500 at room temperature), it is necessary to use ether extraction in order to isolate all of the product. No evidence was found of the presence of a dihydroethoxy naphthoic acid.

The Δ^2-dihydro-α-naphthoic acid was identified by a determination of its neutral equivalent and also by an examination of the product obtained from its rearrangement with alkali. One gram of the acid was boiled for thirty minutes with 25 cc. of 10% potassium hydroxide solution and it was found that this treatment rearranged it completely into the Δ^1-dihydro acid.[3] The Δ^1-dihydro-α-naphthoic acid was identified by its melting point (121°) and its solubility behavior.

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[1] THIS JOURNAL, 38, 419 (1916).

[2] *Ibid.*, 39, 395 (1917).

[3] Cf. Kamm and McClugage, THIS JOURNAL, 38, 427 (1916).