

The Hydrogenation of 3-Methylphthalide

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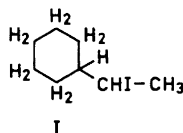
In order to prepare a substance containing a γ -lactone ring condensed with a cyclohexane ring 3-methylphthalide was hydrogenated catalytically. The product obtained, a liquid boiling at 130–131°C at 10 mm Hg, showed in the infra-red two bands in the carbonyl region, *viz.* 1702 and 1777 cm^{-1} , corresponding to a free carboxyl group and a γ -lactone ring, respectively. The liquid could accordingly be separated in two parts by treatment with a solution of sodium carbonate. Part A (60 %) being insoluble in sodium carbonate was a liquid boiling at 130–131°C at 10 mm Hg. This substance was obviously *cis*-3-methylhexahydrophthalide as it could be oxidised by means of sodium hypobromite to cyclohexane-*cis*-1,2-dicarboxylic acid.

Part B (40 %) which had dissolved in sodium carbonate could be recovered as a liquid by adding mineral acid. It distilled at 134–135°C at 10 mm Hg and afterwards crystallized spontaneously. The m.p. was 35–37°C and the substance was found to be identical with the acid obtained by hydrogenating 2-ethylbenzoic acid. The 2-ethyl-cyclohexanecarboxylic acid has not been described in the literature and one cannot therefore *a priori* know if the acid with m.p. 35–37° is the *cis* or *trans* isomer. As the lactone (part A) was shown to be the *cis* isomer it would seem probable that the acid m.p. 35–37° is the *trans* isomer

formed by a continued hydrogenation of the less stable *trans* lactone.

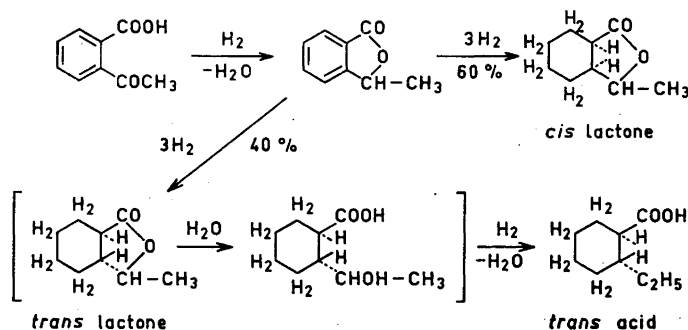
This could be verified if it were possible to transform the *cis* lactone into the corresponding *cis* 2-ethylcyclohexanecarboxylic acid. We have unsuccessfully tried to prove this by using the following two methods. According to Henecka¹ a γ -lactone reacts with ethanolic hydrogen bromide forming a bromo ester in which the bromine could be removed by reduction. In our case, however, no reaction took place with the ethanolic hydrogen bromide. Giebe² found that 3-methylphthalide by treatment with hydrogen iodide and yellow phosphorus gave 2-ethylbenzoic acid, a result which we could verify. When the above *cis* lactone (part A) was treated in the same way no ethylcyclohexanecarboxylic acid was ob-

tained, but a decarboxylation took place and a halogenide $\text{C}_8\text{H}_{15}\text{I}$ was isolated in good yield. The structure of the halogenide is most likely as shown in formula I.



On catalytic hydrogenation of acetophenone-*o*-carboxylic acid the same products were obtained as when starting with 3-methylphthalide. Accordingly the hydrogenation of both substances could be expressed by the scheme below.

Experimental. Hydrogenation of acetophenone-*o*-carboxylic acid. A solution of 5 g acetophenone-*o*-carboxylic acid in 50 ml glacial acetic acid to which 0.5 g platinum oxide had been added was shaken for 15 h with hydrogen at 20°C and 760 mm Hg. In all 3310 ml hydrogen was taken up. On the assumption that 60 % of the starting material had consumed 4 mole and 40 % 5 mole hydrogen the calculated consumption would be 3320 ml. After removing solvent and



catalyst the residue distilled at 130–131° and 10 mm Hg. Yield 4.7 g.

Hydrogenation of 3-methylphthalide. When hydrogenating 3-methylphthalide as described above, the same product in the same yield was obtained. The infra-red spectra were identical in the two cases.

Separation of the two products of hydrogenation. The hydrogenation product (3 g) dissolved in 50 ml ether was shaken for 5 min with 20 ml 2 N sodium carbonate solution. From the ethereal solution, which had been dried with sodium sulphate 1.7 g oil was isolated which distilled at 130–131°C, 10 mm Hg. The equivalent weight was determined by heating samples dissolved in ethanol for some time with 0.1 N sodium hydroxide and back-titrating with hydrochloric acid. (Found: C 69.76; H 8.84; M 154, 155. Calc. for $C_9H_{14}O_2$: C 70.09; H 9.15; M 154.2). n_D^{20} 1.4748, d_4^{20} 1.0595, $[MR]_{\text{found}}$ 40.98. Hexahydro-3-methylphthalide $[MR]_{\text{calc}}$ 41.03.

The aqueous solution was acidified with hydrochloric acid and extracted with ether. An oil was obtained, which after distillation at 134–135°, 10 mm Hg, crystallized. M.p. 35–37°C. Yield 1.1 g. The substance could be titrated as an acid.

(Found C 68.94; H 10.13; M 156, 153. Calc. for $C_9H_{16}O_2$: C 69.18; H 10.33; M 156.2). n_D^{20} 1.4648, d_4^{20} 1.015, $[MR]_{\text{found}}$ 42.85. Ethylcyclohexanecarboxylic acid $[MR]_{\text{calc}}$ 43.12.

For further identification of the acid its *p*-bromophenacyl ester was prepared in the usual way. After recrystallization from ethanol m.p. 70–71°C. (Found: C 57.74; H 5.90; Br 22.26. Calc. for $C_{17}H_{21}O_3Br$: C 57.80; H 5.99; Br 22.61).

The m.p. was not depressed on mixing with the *p*-bromophenacyl ester of the acid obtained by hydrogenation of 2-ethylbenzoic acid.

Oxidation of the lactone (part A) with sodium hypobromite. To an ice-cold solution of 9.5 g sodium hydroxide in 150 ml water 12.5 g bromine were added in small portions. The lactone (2.5 g) was dissolved in 15 ml 2 N sodium hydroxide and the two solutions mixed and left at room temperature until the next day. The bromoform formed was extracted with ether and the solution after adding hydrochloric acid again extracted with ether. After removing excess of bromine with sodium sulphite and drying with sodium sulphate the ether was distilled off. The remaining yellow oil (0.5 g) crystallized partly. After washing with benzene and recrystallization from water the substance had m.p. 189–193°C. The *cis*-cyclohexane-1,2-dicarboxylic acid has, according to the literature, m.p. 192°.

Reduction of the lactone with hydrogen iodide. The lactone $C_9H_{14}O_2$ (7.25 g), 25 ml hydrogen iodide (1.7) and 2.9 g of yellow phosphorus were refluxed for 10 h. A yellow layer which formed on top of the solution was isolated, washed with water saturated with sulphur dioxide and dried in a desiccator. After distilling at 49–52°C at 0.15 mm Hg the liquid weighed 6.6 g.

367.0 and 313.7 mg subst. gave 362.1 and 308.7 mg AgI, respectively. (Found I 53.33, 53.20 %. Calc. for $C_8H_{15}I$ I 53.30 %). n_D^{20} 1.5300, d_4^{20} 1.462, $[MR]_{\text{found}}$ 50.09, $[MR]_{\text{calc}}$ 49.76.

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1. Henecka, H. In Houben-Weyl: *Methoden der organischen Chemie*, 1952, Vol. 8, p. 528.
2. Giebe, G. *Ber.* **29** (1896) 534.

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Determination of the Configuration of β -Amino and β -Hydroxy Acids by Means of Optical Rotatory Dispersion

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It has recently been shown by Sjöberg, Fredga and Djerassi¹, that the absolute configuration of α -amino and α -hydroxy acids can be readily derived from the sign of the Cotton effect in the anomalous rotatory dispersion curves of the dithio-

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