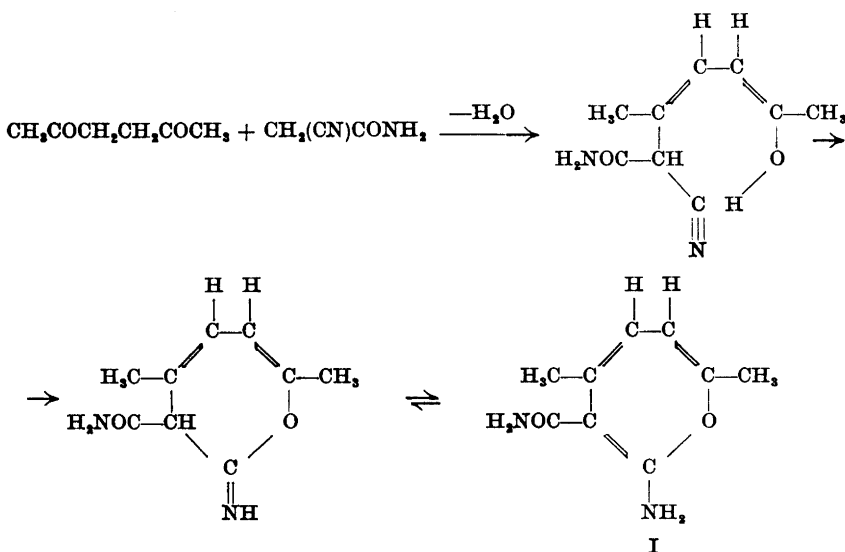


The Preparation of an Oxacycloheptatriene

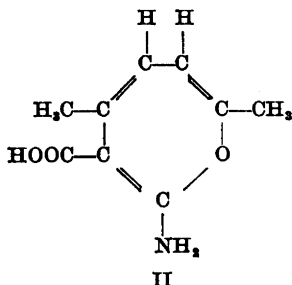
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In alkaline solution acetylacetone reacts with cyanoacetamide with formation of a seven-membered ring, 2-amino-4,7-dimethyloxepine-3-carboxamide (I), according to the equation:



I is a weak base and can be titrated with perchloric acid in anhydrous medium. The structure I of the compound is supported by its IR spectrum, which has no nitrile band and only one C=O band at 1670 cm^{-1} , belonging to the CONH_2 group.



When I is boiled with concentrated hydrochloric acid, the amide group is hydrolysed, the amino acid II being formed.

Experimental. Preparation of 2-amino-4,7-dimethyloxepine-3-carboxamide (I). Acetylacetone (5.0 g) and cyanoacetamide (3.75 g) were dissolved in alkaline ethanol (10 ml of ethanol and 5 ml of 2.4 N sodium hydroxide solution) and allowed to stand overnight. The slightly yellow crystals formed were filtered and washed with 50% ethanol. Yield 2.3 g. The product can be recrystallized from ethanol.

M. p. about 222° (decomp.). (Found: C 60.0; H 6.7; N 15.4; O 17.7; equiv. wt. on titration with perchloric acid in acetic acid — chlorobenzene solution using methyl violet as indicator: 181. Calc. for $\text{C}_9\text{H}_{12}\text{N}_2\text{O}_2$: C 60.0; H 6.7; N 15.5; O 17.8; equiv. wt. 180.) UV absorption: λ_{max} = 233, 277 and 345 μ .

Hydrolysis of I to form 2-amino-4,7-dimethyloxepine-3-carboxylic acid (II). A solution of I (5.0 g) in concentrated hydrochloric acid (75 ml) was boiled for 30 min. The acid was evaporated under reduced pressure and the dry residue was treated with water (75 ml). Sodium acetate solution was added until pH about 3 to make the precipitation of II complete. The precipitate was filtered and washed with water and ethanol. Yield 0.8 g. The product was purified by extraction of by-products with boiling ethanol for half a minute

and by recrystallization from ethanol (solution in excess of hot ethanol as rapidly as possible and evaporation of part of the solvent under reduced pressure to avoid decomposition by heat). M. p. 149° (decomp.). (Found: C 59.8; H 6.2; N 7.8; O 26.3; equiv.wt. by titration using thymolphthalein as indicator: 181. Calc. for $C_9H_{11}NO_3$: C 59.7; H 6.1; N 7.7; O 26.5; equiv.wt. 181.) The IR curve shows amino and carboxyl bands. UV absorption: $\lambda_{max.} = 235, 284$ and 350μ .

The financial support of *Statens naturvetenskapliga forskningsråd* is gratefully acknowledged.

Received February 18, 1959.

o-Methoxybenzhydrol

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o-Methoxybenzhydrol has been prepared by Stoermer and Friderici¹ by reacting *o*-methoxybenzaldehyde with phenylmagnesium iodide. Kahil and Nierenstein², who verified the results of Stoermer and Friderici, obtained the compound also by reduction of *o*-methoxybenzophenone. In both cases the melting point was reported to be 141°. Martynoff³, who synthesized *o*-methoxybenzhydrol from *o*-methoxybenzaldehyde and phenylmagnesium iodide, did not report any melting point but used the crude product for the preparation of bis-*o*-methoxybenzhydrol ether.

When the experiment of Stoermer and Friderici was repeated in this laboratory with *o*-methoxybenzaldehyde and phenylmagnesium bromide the statements as to the melting point of *o*-methoxybenzhydrol could not be verified. Instead of a solid substance, an oil, b.p. 181–182°/8 mm, was obtained. The same substance was formed when *o*-methoxybenzophenone was reduced with zinc in alkaline ethanol. The identity of the oil with *o*-methoxybenzhydrol was established by preparing its 3,5-dinitrobenzoic acid by oxidizing it to *o*-methoxybenzophenone.

o-Methoxybenzhydrol can be heated in boiling xylene for several hours without any change. However, if a minute quantity of an acid is added to the solution, the substance is rapidly and quantitatively

converted into bis-*o*-methoxybenzhydrol ether, m. p. 137–137.5°. This property seems to be the reason for the incorrect melting points reported previously.

When the products of the reaction between *o*-methoxybenzaldehyde and phenylmagnesium bromide were decomposed with ice and hydrochloric acid, a small quantity of bis-*o*-methoxybenzhydrol ether was isolated in spite of the fact that the reaction products were almost immediately treated with a potassium carbonate solution. If the decomposition was effected by adding ammonium chloride solution, the yield of the alcohol was slightly greater and no ether could be isolated. These observations demonstrate the instability of the alcohol towards acids.

Considering the difference in stability in the presence and absence of acids, it seems probable that the crude *o*-methoxybenzhydrol that Martynoff used in his synthesis of bis-*o*-methoxybenzhydrol ether contained a small quantity of acid.

Experimental. To a cooled Grignard reagent prepared from magnesium (3.60 g) and bromobenzene (23.55 g) in dry ether (60 ml), *o*-methoxybenzaldehyde (13.60 g) in dry ether (50 ml) was gradually added. After the mixture had been warmed in a water bath for 15 min, the products were decomposed by pouring them into a mixture of ice and dilute hydrochloric acid. The ether phase was thoroughly washed with water and a dilute potassium carbonate solution. After drying with sodium sulphate, the ether was evaporated and the residue distilled under reduced pressure. The yield of *o*-methoxybenzhydrol, b. p. 181–182°/8 mm, was 77.5 % (16.61 g). (Found: C 78.37; H 6.45. Calc. for $C_{14}H_{14}O_2$: C 78.48; H 6.59.)

The residue in the distillation flask was dissolved in a small quantity of ethanol. After a while bis-*o*-methoxybenzhydrol ether (1.26 g) crystallized. It melted after recrystallization from ethanol at 137–137.5°.

When the decomposition of the reaction products was effected with ammonium chloride solution, the yield of the alcohol was almost 80 % (17.04 g) and no bis-*o*-methoxybenzhydrol ether could be isolated. In this case the washing with potassium carbonate solution was omitted.

A sample of *o*-methoxybenzhydrol was treated with the equivalent quantity of 3,5-dinitrobenzoyl chloride in benzene and pyridine. After the solution had stood for several hours, the precipitate was filtered off and the filtrate washed with water, dilute hydrochloric acid,