142° (18 mm.).[5] The phenolic ketone (84 g.) obtained from several runs was methylated by refluxing for four hours with dimethyl sulfate (44 g.) and 10% sodium hydroxide solution (280 ml.). After processing and fractionation there was obtained 62 g. (70%) of the desired product which boiled at 150-152° (9 mm.).

Anal. Calcd. for $C_{11}H_{13}O_2Cl$: C, 62.16; H, 6.16. Found: C, 62.05; H, 6.26.

The 2,4-dinitrophenylhydrazone melted at 148-149°.

Anal. Calcd. for $C_{17}H_{17}O_5N_4Cl$: C, 51.98; H, 4.36. Found: C, 52.01; H, 4.63.

2-Methoxy-5-bromoisobutyrophenone (II).—Aluminum chloride (60 g.) was dissolved in nitrobenzene (250 ml.) and cooled to −4°. Isobutyryl chloride (48 g.) was added rapidly; then *p*-bromoanisole (84 g.) was dropped in during two hours keeping the temperature at 0°. The mixture was allowed to stir for four hours while the temperature was gradually raised to 15°. Processing produced 74 g. (64%) of the ketone which boiled at 158-163° (10 mm.).

Anal. Calcd. for $C_{11}H_{13}O_2Br$: C, 51.38; H, 5.10. Found: C, 50.93; H, 5.31.

The 2,4-dinitrophenylhydrazone melted at 154-155°.

Anal. Calcd. for $C_{17}H_{17}O_5N_4Br$: C, 46.70; H, 3.92. Found: C, 46.39; H, 4.21.

When aluminum chloride (100 g.) was added to a mixture of *p*-bromoanisole (106 g.) and isobutyryl chloride (62 g.) in carbon disulfide (1200 ml.) at 5° and the mixture allowed to stand at room temperature for two days, there was obtained after processing 48 g. (35%) of demethylated ketone, b. p. 144-155° (12 mm.). This material was dissolved in sodium hydroxide solution and methylated as for the previous ketone to give II, 44 g. (85%).

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[5] von Auwers, Baum and Lorenz, ref. 4, report the boiling point as 130° at 20 mm.

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The Action of 2,4-Dinitrophenylhydrazine on 6-Halogeno-Δ^4-cholestenones

BY D. H. R. BARTON[1] AND E. MILLER

Recently it was reported[2,3] that the action of 2,4-dinitrophenylhydrazine on the 6α- and 6β-chloro- and bromo-Δ^4-cholesten-3-ones in cold methanolic solution afforded an orange compound to which the molecular formula $C_{33}H_{48}N_4O_5$ was assigned. Further examination of this substance has shown that it contains no hydroxyl group (failure to acetylate; no band in infrared), but does contain a C=N grouping and a N-H grouping (infrared maxima at 6.16 and 3.03 μ, respectively, in chloroform solution) and a methoxyl group (Zeisel determination). Having regard to these facts and to the data previously recorded[2,3] we should like to propose the formula 6(α?)-methoxy-Δ^4-cholesten-3-one 2,4-dinitrophenylhydrazone for the orange compound and revise its molecular formula to $C_{34}H_{50}N_4O_5$.

It seems to us that the formulation of this substance is explained somewhat better by the suggestions of Mattox and Kendall[4,5] with regard to the mechanism of the 2,4-dinitrophenylhydrazine reaction with halogeno ketones, at least in ethanol solution, rather than by the alternative proposals of Djerassi,[6] which may apply only for reactions carried out in acetic acid.

Our previous observation[2] that the orange compound was obtained using ethanol and dioxane as solvents must be ascribed to the conditions of working up the reaction product. In each case the orange compound was filtered, washed with the same solvent as had been used for its preparation, and dried. The dry solid was dissolved in a small volume of chloroform and precipitated with methanol. This procedure was repeated once or twice more. The compound thus obtained was dried, dissolved in benzene and chromatographed. It was finally recrystallized very slowly from chloroform-methanol. Presumably etherification or trans-etherification occurred during one of the stages of this involved procedure.[7]

Experimental

For the orange compound prepared as described previously[2]: *Anal.* Calcd. for $C_{34}H_{50}N_4O_5$: C, 68.64; H, 8.48; N, 9.42; Cl, 0.00; OMe, 5.22. Found: C, 68.3^2; H, 8.3^2; N, 9.9^2; Cl, 0.0^2; OMe, 5.10, 5.17.

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[1] Harvard University Visiting Lecturer, 1949-1950.

[2] Barton and Miller, THIS JOURNAL, **72**, 370 (1950).

[3] Barton and Miller, *ibid.*, **72**, 1066 (1950).

[4] Mattox and Kendall, *ibid.*, **72**, 2290 (1950).

[5] We are indebted to Dr. Mattox for kindly sending us a copy of this paper prior to its publication.

[6] Djerassi, THIS JOURNAL, **71**, 1003 (1949).

[7] It is noteworthy that the absorption maximum in the u. v. of the 6-methoxy dinitrophenylhydrazone is somewhat displaced with respect to that for Δ^4-cholestenone dinitrophenylhydrazone.

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The Mannich Reaction with *o*-Phenylphenol

BY J. H. BURCKHALTER[1]

During the preparation of various Mannich phenols for antimalarial study,[2] three substances were isolated as their hydrochlorides from the reaction between equivalent amounts of 2-phenylphenol, paraformaldehyde and diethylamine. Two of these products are the isomeric α-diethylamino-6-phenylcresols (I and II); the third, α^2,α^4-bis-(diethylamino)-6-phenyl-2,4-xylenol (III), is the exclusive product when an excess of paraformaldehyde and diethylamine is used.[2]

One of the isomeric bases responds to Millon's test for an unsubstituted position ortho to a phenolic hydroxyl group and is therefore assigned the structure II. The other isomer is insoluble in dilute sodium hydroxide and should therefore have the structure I.[2,3] The structure of I was

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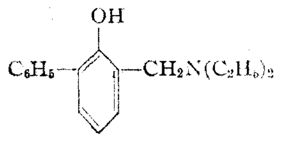
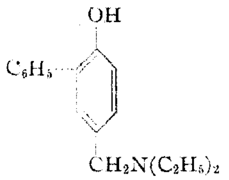
[2] Burckhalter, Tendick, Jones, Holcomb and Rawlins, THIS JOURNAL, **68**, 1894 (1946).

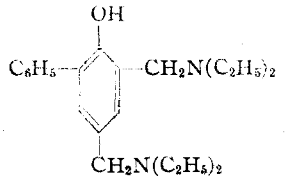
[3] Decombé, *Compt. rend.*, **196**, 866 (1933).



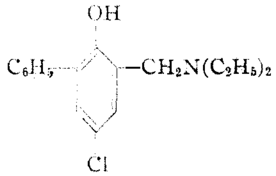
I



II



III



IV

confirmed by synthesizing it from 4-chloro-α-diethylamino-6-phenyl-*o*-cresol (IV).[2] However, attempts to prepare isomer II from 2-chloro-α-diethylamino-6-phenyl-*p*-cresol (V)[2] were unsuccessful.

The Mannich phenols IV and V were prepared from 4-chloro-2-phenylphenol and 2-chloro-6-phenylphenol, respectively.[2] It is important to note that the structures of the starting materials given in the patent literature[4] should be interchanged.[5] These intermediates, the former a liquid and the latter a solid, are properly labeled by the Eastman Kodak Company.

Experimental

Reaction of *o*-Phenylphenol with Formaldehyde and Diethylamine.—A mixture of 6 moles of *o*-phenylphenol, 850 ml. of alcohol, 6 moles of diethylamine and 6 moles of 36% formaldehyde, added in order, was heated for three hours on a steam-bath, during which time the solvent was allowed to distil. After the addition of 500 ml. of water, the mixture was extracted with 1500 ml. of ether, and the ether layer was extracted three times with 500-ml. portions of 2 *N* sodium hydroxide.

The alkaline extract was washed with ether and then treated with 450 ml. of concd. hydrochloric acid, giving a white crystalline solid which was triturated with acetone. The crude product, weighing 278 g., was recrystallized from methanol, giving 228 g. (13% yield) of the pure hydrochloride melting at 223–225°. This compound is soluble in dilute alkali and gives a positive Millon test, indicating that it is the hydrochloride of isomer II.

Anal. Calcd. for $C_{17}H_{21}NO{\cdot}HCl$: C, 69.97; H, 7.60. Found: C, 69.89; H, 7.48.

The original alkaline-extracted ether solution was washed with water, dried over potassium carbonate, filtered and treated with an excess of alcoholic hydrogen chloride. The precipitated mixture of hydrochlorides melted at 147–170° and weighed 1138 g. The ether filtrate gave another 3.8 g. of hydrochloride melting at 148–149°. Fractional crystallization of the mixture of hydrochlorides from acetone, isopropyl or ethyl alcohol gave 740 g. of a pure hydrochloride melting at 148–149° (42% yield) and 106 g. of a second pure hydrochloride melting at 204–206° (8.5% yield). The 204–206° compound is the dihydrochloride of substance III.[2] The 148–149° compound is insoluble in alkali, fails to give Millon's test and must therefore be the hydrochloride of isomer I.

Anal. Calcd. for $C_{17}H_{21}NO{\cdot}HCl$: C, 69.97; H, 7.60. Found: C, 70.27; H, 7.32.

Conversion of 4-Chloro-α-diethylamino-6-phenyl-*o*-cresol (IV) to α-Diethylamino-6-phenyl-*o*-cresol (I).—The free base IV was obtained by treating a water solution of 30 g. of the hydrochloride[2] with excess ammonia. The solid product, washed with water and recrystallized from alcohol, gave 23 g. (87%) of IV melting at 69–70°.

Anal. Calcd. for $C_{17}H_{20}ClNO$: N, 4.83. Found: N, 5.01.

Four grams of sodium, in small pieces, was added during the course of one hour to a solution of 5.8 g. of IV in 100 ml. of boiling amyl alcohol. After refluxing for another hour, a little methanol was added to react with the unchanged sodium, concd. hydrochloric acid added in excess, the amyl alcohol steam distilled and the residue extracted with ether. Excess ammonia was added to the acid layer and the liberated base was extracted with ether. The ether solution of the base was washed, dried and treated with excess alcoholic hydrogen chloride. Recrystallization of the precipitated hydrochloride gave 1.4 g. (24%) of white solid melting at 148–149°. A mixed melting point with the 148–149° product obtained directly by the Mannich reaction proved their identity.

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[4] Britton and Bryner, U. S. Patent 1,969,963; *C. A.*, **28**, 6160 (1934).

[5] Weissberger and Salminen, THIS JOURNAL, **67**, 58 (1945).

An Azeotrope between Paraffin Hydrocarbons

BY GEORGE CALINGAERT[1] AND MIECZYSLAW WOJCIECHOWSKI

The occurrence of azeotropism is based on the existence of a deviation from ideality sufficient to overcome the difference in volatility of the two components of the system. Since deviations from ideality are caused by dissimilarity between molecular species,[2] azeotropism is seldom observed between similar materials, and no report is known of a case of azeotropism between isomers.

A publication from this Laboratory[3] gives data on the deviation from ideality for several binary systems of hydrocarbons. In the case of benzene and cyclohexane the observed total pressure exceeded that calculated for ideality by as much as 8% in the middle of the pressure–composition diagram. This fact, coupled with the proximity of the boiling points of the two components, implied the likelihood of existence of an azeotrope, and this was later confirmed experimentally by Scatchard, Wood and Mochel.[3,4] Definite deviations from ideality were observed between chemical homologs, such as paraffin hydrocarbons, and even between isomeric paraffins, though in the latter case the deviations were only of the order of 1% or less. The possibility of existence of azeotropism even then is not excluded, if the vapor pressures of the two components are sufficiently close together. It was thought that such a pair might be found in 2,2,3-trimethylbutane and 2,4-dimethylpentane, which not only boil less than 0.4° apart under atmospheric pres-

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[1] Hobart and William Smith Colleges, Geneva, N. Y.

[2] B. J. Mair, A. R. Glasgow, Jr., and F. D. Rossini, *J. Res. Natl. Bur. Standards*, **27**, 39 (1941).

[3] H. A. Beatty and G. Calingaert, *Ind. Eng. Chem.*, **26**, 504 (1934).

[4] G. Scatchard, S. E. Wood and J. M. Mochel, *J. Phys. Chem.*, **43**, 119 (1939).