Diethylcyclohexylamine was prepared from cyclohexylamine and diethyl sulfate. Primary and secondary amines were removed with benzenesulfonyl chloride. The product boiled at 68.5–69 at 10 mm.; neut. equiv. calcd. 155.3, found 156.1.

Cyclohexanol was prepared from diethylcyclohexylamine in 33% yield under the conditions used for the hydrolysis of cyclohexylamine. Seventy-eight grams of diethylcyclohexylamine was treated with 300 ml. of 50% aqueous dioxane and 23 g. of copper–chromium oxide catalyst at 270–280° without hydrogen pressure. The product boiling at 50–68° at 10 mm. was acidified and extracted with ether. Only about 1 g. of neutral material was obtained. The amine hydrochlorides were treated with alkali and the free amines fractionated at 10 mm. The fraction boiling at 53.5–56° weighed 12 g. and gave a neutral equivalent of 133.0 (calculated for mono- and diethylcyclohexylamines, 127.2 and 155.3, respectively). This product on treatment with sodium nitrite and hydrochloric acid yielded 5 g. of a pale yellow oil, b. p. 127–128° at 12.5 mm. The literature[6] gives 130° at 12 mm. as the boiling point of N-nitrosoethylcyclohexylamine.

Summary

1. A number of new piperazine derivatives have been prepared from amino alcohols by catalytic alkylation.

2. The formation of alcohols from amines under catalytic alkylation conditions has been reported. This side reaction may account in part for the poor yields obtained in certain alkylations.

3. The generality and applicability of this reaction is being studied.

(6) Heilbron, "Dictionary of Organic Compounds," Vol. II, 1936, p. 27.

GAINESVILLE, FLORIDA RECEIVED JULY 13, 1939

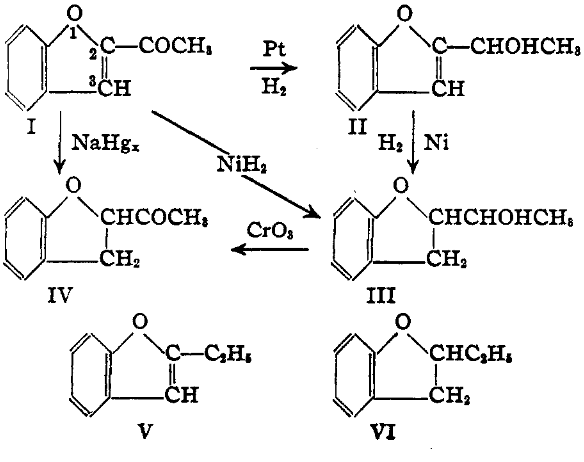
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Derivatives of Coumaran. VI. Reduction of 2-Acetobenzofuran and its Derivatives

BY R. L. SHRINER AND JOHN ANDERSON

In an investigation concerned with the preparation of 2-substituted coumarans, the catalytic hydrogenation of 2-acetobenzofuran and some of its derivatives was studied.

It has been found possible to obtain the two alcohol reduction products of 2-acetobenzofuran (I) by catalytic hydrogenation provided the appropriate catalyst is employed. Hydrogenation with a platinum catalyst results in the formation of 2-(1-hydroxyethyl)-benzofuran (II) while a Raney nickel catalyst leads to the formation of 2-(1-hydroxyethyl)-coumaran (III). The coumaran (III) also can be obtained from the benzofuran (II) by hydrogenation in the presence of Raney nickel.



Hydrogenation in the presence of colloidal platinum resulted in a mixture of II, III, 2-ethylbenzofuran (V) and 2-ethylcoumaran (VI). No 2-acetocoumaran (IV) was found among the products of catalytic reduction. A sample of this ketone was made by oxidation of the alcohol (III) and by a sodium amalgam reduction of 2-acetobenzofuran. It was characterized by its semicarbazone.

The catalytic reduction of 2-acetobenzofuran thus follows a course different from that of the closely related benzalacetone, which is smoothly reduced to benzylacetone[1] first and then undergoes further reduction to 4-phenyl-2-butanol. The results constitute further evidence that catalytic hydrogenation of α,β-unsaturated ketones occurs by 1,2-addition[1] and not by 1,4-addition[2] as is the case in reduction by chemical means.[3] In this particular case the double bond in the 2,3-position probably is stabilized to some extent by resonance in the benzofuran nucleus.

ω-Acetoxy-2-acetobenzofuran (VIII) was prepared by bromination of 2-acetobenzofuran, followed by treatment of the resulting ω-bromo-2-acetobenzofuran (VII) with sodium acetate.

An unusual reaction took place when ω-acetoxy-2-acetobenzofuran (VIII) was subjected to

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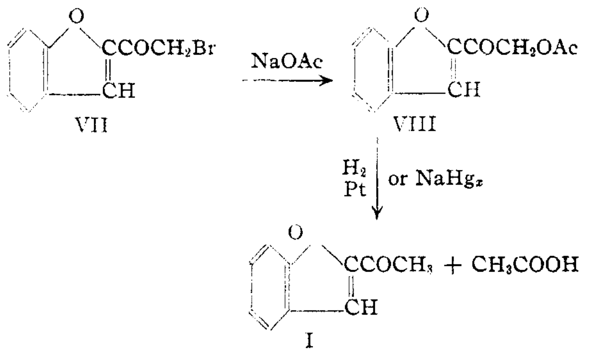
(1) Kern, Shriner and Adams, THIS JOURNAL, **47**, 1147 (1925).

(2) Straus and Grindel, *Ann.*, **439**, 276 (1924).

(3) Conant and Cutter, *J. Phys. Chem.*, **28**, 1105 (1924).



catalytic hydrogenation. It was found that the major portion of the reacting material underwent cleavage to acetic acid and 2-acetobenzofuran (I). In the reductions when only one mole of hydrogen was absorbed, 2-acetobenzofuran was obtained as the cleavage product while mixtures of reduction products of 2-acetobenzofuran were obtained when more than one mole of hydrogen was absorbed. Sodium amalgam reduction of ω-acetoxy-2-acetobenzofuran in acetic acid solution resulted in a similar cleavage producing a mixture of the reduction products of 2-acetobenzofuran.

It seemed possible that this cleavage reaction might be general for phenacyl esters but catalytic reduction of phenacyl acetate in the presence of platinum oxide gave a good yield of 1-phenyl-2-acetoxyethanol and only a very small amount of methylphenylcarbinol and acetic acid.

Experimental

2-Acetobenzofuran.—This substance was prepared from salicylaldehyde and chloroacetone according to the method of Stoermer, Chydenius and Schinn.[4] A 60% yield of colorless crystals melting at 74–75° was obtained.

ω-Bromo-2-acetobenzofuran.—The method for the preparation of this compound was indicated by Calov and Stoermer[5] but these authors gave neither detailed directions for the preparation nor analysis of the product. A solution of 25.0 g. of bromine in 200 cc. of carbon disulfide was added dropwise, with stirring, into a solution of 25.0 g. of 2-acetobenzofuran in 200 cc. of the same solvent. The bromine was added during a period of two hours and at the end of this time the carbon disulfide was removed by evaporation to leave a yellow solid residue. The pure product, which exists in the form of white needles with a melting point of 90–91°, was obtained in a yield of 34 g. by recrystallizing the residue twice from ethanol. The yield was 91% of the theoretical.

Anal. Calcd. for $C_{10}H_7BrO_2$: C, 50.24; H, 2.95; Br, 33.42. Found: C, 50.52; H, 3.16; Br, 33.25.

ω-Acetoxy-2-acetobenzofuran.—A solution of 50 g. of sodium acetate trihydrate, 25.0 g. of ω-bromo-2-acetobenzofuran and 5 cc. of 6 *N* hydrochloric acid in 500 cc. of 50% ethanol was refluxed for one and a half hours. The mixture was poured into 500 cc. of ice water and the crude product was removed by filtration. The product was purified by recrystallization from ethyl acetate to give 17 g. (74%) of yellow needles which had a melting point of 86–87°.

Anal. Calcd. for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62. Found: C, 66.29; H, 4.72.

2-(1-Hydroxyethyl)-benzofuran.—A mixture of 16.0 g. of acetobenzofuran in 100 cc. of absolute ethanol and 0.1 g. of platinum oxide was shaken in an atmosphere of hydrogen at a pressure of 2 to 3 atmospheres for six hours. At the end of this time one mole of hydrogen had been absorbed and the absorption had ceased. The catalyst was removed by filtration and the ethanol was removed by distillation from an oil-bath at 150°. The residue solidified to give the product, which had a melting point of 41°, in a quantitative yield. Recrystallization of the product by dissolving it in a small amount of ether at room temperature and cooling in a dry ice–acetone bath did not raise the melting point. The product boiled at 147° under a pressure of 19 mm. but purification by distillation did not raise the melting point.

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Found: C, 74.25; H, 6.33.

The phenylurethan of the product was prepared by heating equimolecular quantities of the alcohol and phenyl isocyanate on a steam-bath for five hours. The mixture was taken up in carbon tetrachloride and filtered. Evaporation of the carbon tetrachloride at room temperature caused precipitation of the phenylurethan in crystalline form. It was recrystallized from a mixture of one part of benzene and two parts of low-boiling petroleum ether to give white needles with a melting point of 102–103°.

Anal. Calcd. for $C_{17}H_{15}NO_3$: N, 4.98. Found: N, 5.11.

Previous investigators[6] described 2-(1-hydroxyethyl)-benzofuran and its phenylurethan but the alcohol was reported to have a melting point of 37° and the phenylurethan to have a melting point of 126°.

2-(1-Hydroxyethyl)-coumaran from 2-(1-Hydroxyethyl)-benzofuran.—To a solution of 8 g. of 2-(1-hydroxyethyl)-benzofuran in 100 cc. of absolute ethanol there was added 2 g. of Raney nickel. The mixture was shaken in an atmosphere of hydrogen at a pressure of two to three atmospheres. One mole of hydrogen was absorbed in fourteen hours and the absorption ceased. The ethanol was removed by distillation and the residue subjected to vacuum distillation. The entire residue distilled at 145° under a pressure of 20 mm. to yield 6.5 g. (81%) of the product as a colorless, viscous liquid with the following constants: d^{25}_{25} 1.1138; n^{25}_D 1.5470; M_D found 46.7, M_D calcd 45.9.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 72.94; H, 7.38.

This compound was reported by former investigators[6] to have a density of 1.506 at 18°.

The phenylurethan of the above compound was prepared by heating equimolecular quantities of the compound

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[4] Stoermer, Chydenius and Schinn, *Ber.*, **57**, 75 (1924).

[5] Calov and Stoermer, *Ann.*, **312**, 322 (1900).

[6] Stoermer and Shaffer, *Ber.*, **36**, 2869, 2871 (1903).

and phenyl isocyanate on a steam-bath for eight hours. The reaction mixture was taken up in glacial acetic acid and poured into ice water to cause separation of the crude phenylurethan. It was recrystallized from a mixture of one part of benzene and two parts of low-boiling petroleum ether to give white needles which melted at 115–116°.

Anal. Calcd. for $C_{17}H_{17}NO_3$: N, 4.95. Found: N, 5.16.

The phenylurethan of 2-(1-hydroxyethyl)-coumaran was formerly reported[6] to have a melting point of 73° but it seems probable that this was a mixture of the phenylurethans of 2-(1-hydroxyethyl)-coumaran and 2-(1-hydroxyethyl)-benzofuran.

2-(1-Hydroxyethyl)-coumaran from 2-Acetobenzofuran.—To a solution of 25 g. of acetobenzofuran in 120 cc. of absolute ethanol there was added 8 g. of Raney nickel and the mixture was shaken in an atmosphere of hydrogen at a pressure of two to three atmospheres. Two moles of hydrogen was absorbed in thirty-six hours and the absorption ceased. The solution was filtered, the ethanol removed by distillation, and the residue fractionally distilled to yield 22.5 g. of 2-(1-hydroxyethyl)-coumaran which was identical in all its properties with that prepared by hydrogenation of 2-(1-hydroxyethyl)-benzofuran. The yield by this method of preparation was 90% of the theoretical.

Hydrogenation of 2-Acetobenzofuran in the Presence of Colloidal Platinum.—To a solution of 24 g. of 2-acetobenzofuran in 100 cc. of absolute ethanol there was added 1.0 g. of Norite, 0.1 g. of chloroplatinic acid and 0.05 g. of platinum oxide. The mixture was shaken in an atmosphere of hydrogen at a pressure of two to three atmospheres and one mole of hydrogen was absorbed in nine minutes. The catalyst was removed by filtration and the ethanol by distillation. The only pure compound which could be isolated from the residue was unchanged acetobenzofuran.

A second reduction was carried out in which two moles of hydrogen were absorbed. The product was isolated as above and consisted of two definite fractions. The lower-boiling fraction weighed 5.5 g., distilled at 99–100° under a pressure of 19 mm. and had the following constants: d^{20}_{20} 1.0196; n^{20}_{D} 1.5475.

Anal. Calcd. for $C_{10}H_{10}O$: C, 82.16; H, 6.89. Calcd. for $C_{10}H_{20}O$: C, 81.04; H, 8.16. Found: C, 81.92; H, 7.56.

This product was evidently a mixture of 2-ethylbenzofuran and 2-ethylcoumaran. The higher-boiling fraction weighed 7.5 g. and distilled at 144–145° under a pressure of 19 mm. It was a mixture of 2-(1-hydroxyethyl)-coumaran and 2-(1-hydroxyethyl)-benzofuran.

Chromic Anhydride Oxidation of 2-(1-Hydroxyethyl)-coumaran.—To a solution of 14.5 g. of 2-(1-hydroxyethyl)-coumaran in 40 cc. of glacial acetic acid there was added, with stirring, 58.0 g. of a 10% solution of chromic anhydride in glacial acetic acid. The oxidizing solution was added in portions over a period of forty-four hours and the mixture was stirred for twelve hours longer at room temperature and seven hours at 80°. The reaction mixture was poured into 700 cc. of water and the resulting solution was treated with sodium bicarbonate until all of the acetic acid was neutralized. The neutral solution was extracted with 400 cc. of ether in four portions, the ether extract was dried over calcium chloride and the ether removed by evaporation. The methyl ketone portion of the concentrate was then isolated by shaking in saturated sodium bisulfite solution and removing the bisulfite addition compound by filtration. The bisulfite addition product weighed 7 g., which is 29% of the theoretical yield. The bisulfite addition compound was decomposed by shaking it in 2% sulfuric acid, the free ketone was extracted with ether and the ether solution dried over calcium chloride. After the calcium chloride was removed by filtration and the ether by evaporation, the crude ketone was treated with semicarbazide hydrochloride and sodium acetate in ethanol solution in the usual manner and the semicarbazone which formed was recrystallized five times from 50% ethanol to give white needles with a melting point of 168–169°.

Anal. Calcd. for $C_{11}H_{13}N_3O_2$: N, 19.17. Found: N, 19.20.

Since 2-acetocoumaran semicarbazone has been reported[4] to have a melting point of 192°, it was thought advisable to determine the melting point of a mixture of the product described above and 2-acetobenzofuran semicarbazone which would be the impurity most likely to be present in the compound previously described because the investigators had obtained their 2-acetocoumaran from sodium amalgam reduction of 2-acetobenzofuran. It was found that the addition of small quantities of 2-acetobenzofuran semicarbazone (m. p. 217°) to the semicarbazone obtained above raised the melting point to the neighborhood of 190°.

A sodium amalgam reduction of 2-acetobenzofuran, using a much larger excess of sodium amalgam than that given in the directions of Stoermer, Chydenius and Schinn,[4] resulted in the formation of a ketone the semicarbazone of which melted at 168–169° and which proved to be identical with the semicarbazone obtained above.

Hydrogenation of ω-Acetoxy-2-acetobenzofuran. (a) With Platinum Oxide.—A solution of 7.5 g. of ω-acetoxy-2-acetobenzofuran in 60 cc. of absolute ethanol and 1.5 g. of platinum oxide was shaken with hydrogen at 3 atmospheres pressure. One mole equivalent of hydrogen was absorbed in ten minutes and the reaction was stopped at this point. The catalyst was removed by filtration, the solvent distilled and the residue fractionated.

The forerun was treated on a watch glass with piperazine hexahydrate and the piperazonium salt which formed was recrystallized from *n*-butanol. It melted at 208–209° and comparison with an authentic sample of piperazinium diacetate[7] showed that they were identical and proved the presence of acetic acid in the reduction mixture. The main fraction boiled at 147–148° at 20 mm. and solidified on standing. Recrystallization from alcohol yielded 4.2 g. of colorless crystals melting at 74–75° and which were identical with 2-acetobenzofuran.

A second reduction was carried out using only 0.2 g. of catalyst. At the end of forty-eight hours 1.8 mole equivalents had been absorbed.

Fractionation of the products yielded 6.0 g. of a liquid which boiled at 146–148° at 18 mm. and 2.4 g. which boiled at 180–200° at 18 mm. The lower boiling fraction was redistilled and a middle fraction taken for analysis.

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(7) Pollard, Adelson and Bain, THIS JOURNAL, 56, 1759 (1934).

Anal. Calcd. for $C_{10}H_8O_2$: C, 74.99; H, 5.03. Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 74.97; H, 6.64.

The analyses indicate that this material is probably a mixture of acetobenzofuran and its reduction products. Had the acetoxy group not been cleaved, the carbon and hydrogen analyses would both have yielded much lower values.

A third reduction was carried out in which a solution of 10.0 g. of acetoxyacetobenzofuran in 150 cc. of cyclohexane was shaken with hydrogen at 2 to 3 atmospheres pressure in the presence of 5.0 g. of Raney nickel. No hydrogen was absorbed in three hours and 0.1 g. of platinum oxide was added to the reaction mixture. One mole of hydrogen was then absorbed in twenty-four hours and absorption ceased at this point. The catalyst was removed by filtration and the solvent by distillation to leave a residue which solidified. Recrystallization of the residue yielded 4.3 g. of 2-acetobenzofuran.

(b) **With Raney Nickel in Ethanol.**—Hydrogenation with Raney nickel in ethanol at 2 to 3 atmospheres pressure took place slowly. Acetic acid was identified as one product but the remainder consisted of a mixture which could not be separated readily.

Sodium Amalgam Reduction of ω-Acetoxy-2-acetobenzofuran.—To a solution of 10.0 g. of ω-acetoxy-2-acetobenzofuran in 300 cc. of 60% acetic acid there was added in small portions, over a period of twenty-four hours, 600 g. of 3% sodium amalgam. The solution which had been stirred and kept at room temperature throughout the time of addition was then diluted with an equal volume of water, neutralized with the calculated quantity of 5% sodium hydroxide solution and extracted with ether. The ether extract was dried over calcium chloride and the ether was removed by distillation to leave a liquid residue. Fractional distillation of the residue gave a product which weighed 6.2 g. and boiled at 115–130° at 6 mm. Refractionation of this product gave 4.5 g. of material boiling at 115–120° and 1.2 g. boiling at 120–130°. The lower boiling material was again fractionated and the middle portion taken for analysis.

Anal. Calcd. for $C_{10}H_8O_2$: C, 74.99; H, 5.03. Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Found: C, 74.16; H, 6.09.

All portions of the product were treated with semicarbazide hydrochloride and sodium acetate in ethanol solution to yield a semicarbazone which melted at 200–201°. This semicarbazone gave the following analytical data.

Anal. Calcd. for $C_{13}H_{15}N_3O_4$: N, 15.16; C, 56.30; H, 5.42. Calcd. for $C_{11}H_{11}N_3O_2$: N, 19.35; C, 60.81; H, 5.11. Calcd. for $C_{11}H_{13}N_3O_2$: N, 19.17; C, 60.26; H, 5.98. Found: N, 19.38; C, 60.52; H, 5.66.

This semicarbazone is evidently a mixture of the semicarbazones of 2-acetobenzofuran and 2-acetocoumaran. The analyses show that under these conditions the acetoxy group is cleaved in a manner similar to the cleavage in the catalytic hydrogenations and that the ketone portion of the product is a mixture of 2-acetobenzofuran and 2-acetocoumaran.

Hydrogenation of Phenacyl Acetate.—A solution of 25.0 g. of phenacyl acetate in 200 cc. of absolute ethanol was shaken with hydrogen at two to three atmospheres pressure in the presence of 0.2 g. of platinum oxide. One mole of hydrogen was absorbed in three and one-half hours and the reduction was stopped at this point. The catalyst was removed by filtration and the ethanol by distillation. The residue was distilled and 1 cc. of distillate collected. This was treated with piperazine hydrate and the salt which resulted recrystallized from *n*-butanol. It melted at 208–209°, corresponding to piperazinium diacetate. The remainder was fractionally distilled to yield 1.8 g. of material boiling at 90–140° under a pressure of 25 mm. and 19.5 g. of material boiling at 163–168° under a pressure of 25 mm. The main fraction was redistilled and it boiled almost entirely at 136–137° under a pressure of 6 mm. and a middle fraction showed the following constants: d^{20}_{20} 1.1438; n^{20}_D 1.5260; M_D calcd. for 1-phenyl-2-acetoxyethanol, 48.0; M_D found, 48.4.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.80; H, 6.65.

The lower boiling fraction was redistilled and the fraction which boiled at 190–205° was treated with α-naphthyl isocyanate at room temperature for ten hours to give a reaction mixture which was extracted with 250 cc. of petroleum ether. The petroleum ether extract was evaporated at room temperature to give a crude α-naphthyl urethan which was recrystallized from petroleum ether to give white needles with a melting point of 94–96°. Since this substance was not obtained in sufficient quantities to allow further purification by recrystallization, it was subjected to analysis.

Anal. Calcd. for $C_{19}H_{17}NO_2$: N, 4.81. Found: N, 4.96.

Evidently this lower boiling fraction contained a small amount of phenylmethylcarbinol which formed the above urethan.

Summary

Catalytic reduction of 2-acetobenzofuran with platinum and hydrogen produced 2-(1-hydroxyethyl)-benzofuran. With hydrogen and nickel 2-(1-hydroxyethyl)-coumaran was formed. 2-Acetocoumaran was obtained by a sodium amalgam reduction of 2-acetobenzofuran and by oxidation of 2-(1-hydroxyethyl)-coumaran.

ω-Acetoxy-2-acetobenzofuran was cleaved by reducing agents to 2-acetobenzofuran and acetic acid.

URBANA, ILLINOIS RECEIVED JULY 21, 1939