hours. The red, viscous liquid, extracted with the minimum quantity of boiling benzene, was separated from the water layer. The crystals deposited from the benzene solution after two hours were dissolved in aqueous sodium bicarbonate and the solution decolorized. The solid precipitated upon acidification was recrystallized from aqueous alcohol; m. p. 143–144°; melting point of mixture with authentic 5,7-diethyl-2-phenyl-2-azobicyclo-(2,3,1)-oct-6-ene-3-one-8-carboxylic acid[2] 143–144°; yield, 14–16.5 g. (60–70%).

(2) Similar yields of 5,7-dimethyl-2-phenyl-2-azabicyclo-(2,3,1)-oct-6-ene-3-one-8-carboxylic acid, m. p. 157–158°, were obtained by the use of 2-methyl-2-pentenal.[4]

Anal. Calcd. for $C_{16}H_{17}O_3N$: N, 5.17. Found: N, 5.06.

This product also was prepared by the reaction of the corresponding anil with maleic anhydride. 2-Methyl-2-pentenalaniline was prepared by the method described[2] for 2-ethyl-2-hexenalaniline; b. p. 131–132° (10 mm.). The anil was treated with maleic anhydride as previously described.[2] The condensation product was obtained in 60% yield; m. p. 157.5–158°; a mixed m. p. with a sample prepared from maleanilic acid showed no depression.

Degradation with concentrated sodium hydroxide[2] gave 3,5-dimethylbenzoic acid, m. p. 166–167°; a mixed m. p. with an authentic sample showed no depression.

(3) When N-phenylmaleimide[5] was substituted for maleanilic acid in (1), no product soluble in aqueous sodium bicarbonate was formed.

(4) Repetition of (1) with 10 g. of maleanilic acid, 7 g. of 2-ethyl-2-hexenal, and 1 g. of phenyl isocyanate gave 7 g. (45%) of III, m. p. 141–143°.

(5) When 52 g. of 2,3-dimethylbutadiene was substituted for 2-ethyl-2-hexenal in (1), no reaction was observed and maleanilic acid was recovered.

Summary

The condensation product previously obtained from maleic anhydride and 2-ethyl-2-hexenalaniline is more conveniently obtained by heating a mixture of maleanilic acid and 2-ethyl-2-hexenal. The occurrence of this reaction is considered as evidence that the formation of maleanilic acid and an aldehyde from an anil, maleic anhydride, and water is a reversible process.

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[4] Doebner and Weissenborn, *Ber.*, **35**, 1144 (1902).

[5] Anschütz and Wirtz, *Ann.*, **239**, 142 (1887).

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

The Synthesis of 3,5-Diethylbenzoic Acid

BY H. R. SNYDER, ROBERT R. ADAMS AND A. V. McINTOSH, JR.

An authentic sample of 3,5-diethylbenzoic acid was sought for comparison with that obtained by degradation of the product of condensation of maleic anhydride with 2-ethyl-2-hexenalaniline.[1] Such comparison was desirable in order to eliminate the possibility that the material in hand might be a methylpropylbenzoic acid.

Several methods for the synthesis of 3,5-diethylbenzoic acid were tested. The oxidation of *sym*-triethylbenzene with nitric acid, a procedure which is reasonably satisfactory for the preparation of 3,5-dimethylbenzoic acid from mesitylene,[2] produced a mixture from which a dibasic acid and a keto acid were isolated. From the analyses and the fact that they were produced from *sym*-triethylbenzene, these substances must be 5-ethylisophthalic acid and 3-aceto-5-ethylbenzoic acid. The first was obtained as the residue from extraction of the mixed acids with benzene; the second was isolated by distillation of the methyl esters of the benzene soluble acids. 3,5-Diethylbenzoic acid was also isolated from this fraction, but in yields of only 1–2%.

The alkylation of bromobenzene with ethyl bromide and aluminum chloride was considered a possible route to a precursor of the desired acid. Berry and Reid[3] obtained products described as brominated ethylbenzenes by treatment of bromobenzene with ethylene and aluminum chloride at 70°. It is known that when bromobenzene is heated in the presence of aluminum chloride, disproportionation to benzene and dibromobenzenes occurs.[4] However, Norris and Turner[5] have concluded that in the rearrangement of the chlorotoluenes by aluminum chloride at temperatures of 100° or below, the methyl group migrates more readily than the chlorine atom. It thus appeared possible that 3,5-diethylbromobenzene might be prepared by the low temperature ethylation of bromobenzene. When the experiment

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[1] Snyder, Hasbrouck and Richardson, THIS JOURNAL, **61**, 3558 (1939).

[2] Fittig, *Ann.*, **141**, 144 (1867).

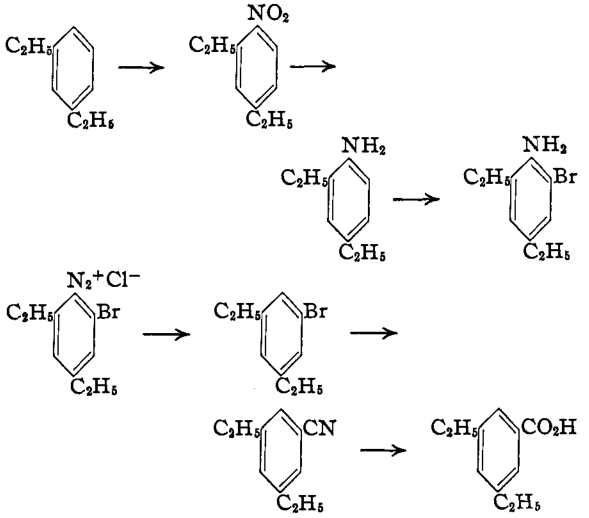
[3] Berry and Reid, THIS JOURNAL, **49**, 3146 (1927).

[4] Copisarow, *J. Chem. Soc.*, **119**, 442 (1921).

[5] Norris and Turner, THIS JOURNAL, **61**, 2128 (1939).

was carried out, employing the procedure used for the preparation of triethylbenzene,[6] the only products isolated were *p*-dibromobenzene and *sym*-triethylbenzene.

The synthesis of 3,5-diethylbenzoic acid from commercial *m*-diethylbenzene, by the sequence of reactions illustrated, proved to be very satisfactory.



The hydrocarbon was nitrated by the method of Copenhaver and Reid,[7] and 2,4-diethylaniline was obtained by catalytic reduction of the nitro compound. Bromination of the amine in a mixture of methyl alcohol and acetic acid gave 6-bromo-2,4-diethylaniline. This was deaminated by diazotization in aqueous acetic acid and treatment of the diazonium chloride with hypophosphorous acid.

3,5-Diethylbromobenzene reacted with magnesium in the presence of ether to give a brown solution. Hydrolysis of samples of this solution and titration with standard acid and alkali[8] indicated the presence of about 75% of the theoretical amount of *sym*-diethylphenylmagnesium bromide. However, carbonation of the solution or treatment with phenyl isocyanate gave the expected products in yields of only 15%. This behavior apparently is due to some unexpected property of 3,5-diethylbromobenzene or its Grignard reagent, for samples of the same lot of 3,5-diethylbromobenzene reacted with anhydrous cuprous cyanide to give 3,5-diethylbenzonitrile in excellent yields. Hydrolysis of the nitrile by the action of sodium hydroxide in diethylene glycol containing a little water gave nearly quantitative yields of 3,5-diethylbenzoic acid.

Experimental

1. Oxidation of Mesitylene with Nitric Acid.—The following modification of Fittig's procedure[2] was employed. A mixture of 25 g. of mesitylene, 48 cc. of concentrated nitric acid and 120 cc. of water was heated under reflux for eighteen hours. The solid which separated from the cold mixture was dissolved in aqueous sodium bicarbonate and freed from neutral material by extraction with ether. After reprecipitation and recrystallization from aqueous ethanol, 6.5 g. (20.5%) of 3,5-dimethylbenzoic acid, m. p. 165.5–166.5°, was obtained.

2. Oxidation of *sym*-Triethylbenzene with Nitric Acid.—When an equal weight of *sym*-triethylbenzene was substituted for mesitylene in the above procedure, 0.3 g. (1%) of 3,5-diethylbenzoic acid was obtained.

A mixture of 25 g. of *sym*-triethylbenzene, 180 cc. of water, and 70 cc. of concentrated nitric acid was stirred vigorously and heated under reflux for five hours. The organic layer was separated from the cold reaction mixture and washed with water. It was dissolved in ether and extracted with two 700-cc. portions of aqueous sodium bicarbonate (10%). Acidification of the extracts gave 8 g. of a semi-solid green substance. This was extracted with 200 cc. of benzene. The residue was recrystallized from aqueous ethanol, yielding 1.7 g. (5.3%) of colorless 5-ethylisophthalic acid, m. p. 265–266°.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.83; H, 5.16; N. E., 97. Found: C, 62.18; H, 5.36; N. E., 97.4.

The residue from evaporation of the benzene solution was heated to reflux with 75 cc. of methanol containing 0.3 cc. of sulfuric acid. After seven hours, 45 cc. of methanol was removed from the solution by distillation through a 12-inch (31-cm.) fractionating column. The residue was diluted with 200 cc. of 1% aqueous sodium bicarbonate solution and the resulting mixture was extracted with two 75-cc. portions of ether. The residue from the removal of the ether from the dried extract was distilled under diminished pressure. The fraction boiling at 106–130° (3.5 mm.) was redistilled and the portion (0.7 g.) boiling at 110–112° (3.5 mm.) was collected as methyl 3,5-diethylbenzoate.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.95; H, 8.40. Found: C, 74.92; H, 8.35.

Saponification of the ester gave 0.5 g. of 3,5-diethylbenzoic acid, m. p. 130°.[9]

In a similar run in which the oxidation was continued for twenty hours the distilled methyl ester contained a colorless solid. After recrystallization from aqueous methanol it melted at 77–78° and weighed 0.8 g. The substance gave a positive iodoform test. Analysis indicates that it was methyl 3-aceto-5-ethylbenzoate.

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.86; H, 6.85. Found: C, 69.82; H, 6.83.

Saponification of the methyl ester (0.3 g.) gave 3-aceto-5-ethylbenzoic acid, m. p., 156–157°.

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[6] Norris and Rubinstein, THIS JOURNAL, **61**, 1166 (1939).

[7] Copenhaver and Reid, *ibid.*, **49**, 3157 (1927).

[8] Gilman, Wilkinson, Fishel and Meyers, *ibid.*, **45**, 150 (1923).

[9] The melting point (133°) reported earlier[1] is in error; the purest samples of 3,5-diethylbenzoic acid have melted sharply at 130°.

Anal. Calcd. for $C_{11}H_{12}O_3$: C, 68.75; H, 6.30; N. E., 192. Found: C, 68.82; H, 6.38; N. E., 187.

3. **Reaction of Bromobenzene and Ethyl Bromide in the Presence of Aluminum Chloride.**—The procedure employed was that of Norris and Rubinstein[6] for the preparation of *sym*-triethylbenzene, except that only two moles of ethyl bromide per mole of bromobenzene was used. The product was distilled through an 18-inch (46.5-cm.) carborundum-packed column[10]; the temperature rose gradually from 208 to 257°. The portion boiling at 208–215° was refractionated and the material (10 g.) collected at 211–212.5° was examined. It was found to have about half the bromine content calculated for diethylbromobenzene. When cooled in dry-ice and acetone, crystals of *p*-dibromobenzene (identified by mixture melting point) separated. These were collected and the liquid remaining was found to boil at 214°; $n^{18.1}D$ 1.4950. This was evidently *sym*-triethylbenzene[11] (b. p. 214.8°, $n^{18.1}D$ 1.4956).

4. **The Preparation of 2,4-Diethyl-6-bromoaniline.**—4-Nitro-1,3-diethylbenzene was prepared from *m*-diethylbenzene (Dow alkazene 3) in 75–80% yields by the method of Copenhaver and Reid.[7] The product boiled at 112–114° (3.8 mm.); $n^{25}D$ 1.5271. The reported values are b. p. 133° (4 mm.); $n^{25}D$ 1.5300. The nitro compound was reduced by hydrogenation over Raney nickel (alcohol solution, temperature 40–60°, pressure 1000–2000 lb.), yielding 80–90% of 2,4-diethylaniline, b. p. 143–144° (38 mm.) $n^{25}D$ 1.5411. The reported values are b. p. 141° (30 mm.) $n^{25}D$ 1.5395. To make certain that the amine was pure, a sample was converted to the acetyl derivative,[7] which was purified by recrystallization. The amine regenerated by hydrolysis of the purified anilide boiled at 142.5° (33 mm.) and had $n^{25}D$ 1.5410.

A solution of 15 g. of 2,4-diethylaniline in 50 cc. of methyl alcohol and 10 cc. of acetic acid was cooled and stirred while 5 cc. of bromine in 50 cc. of acetic acid was added. The temperature of the mixture was kept below 15°. Near the end of the addition the mixture became nearly solid. The solvents were evaporated under diminished pressure and the bromo amine was isolated by treatment with aqueous alkali and extraction with ether, removal of the solvent, and distillation under diminished pressure. The portion boiling at 100–105° (1.5 mm.) weighed 12.5 g. (55%). The yield from runs of ten times this size was about 40%.

Anal. Calcd. for $C_{10}H_{14}NBr$: C, 52.5; H, 6.19. Found: C, 52.3; H, 6.18.

5. **The Preparation of 3,5-Diethylbromobenzene.**—The amino group was replaced by hydrogen by the procedure of Adams and Kornblum.[12] A solution of 77 g. of 2,4-diethyl-6-bromoaniline in 600 cc. of acetic acid, 400 cc. of water and 120 cc. of concentrated hydrochloric acid was diazotized by addition of a solution of 25 g. of sodium nitrite in 150 cc. of water. The temperature was maintained at 5–8°. The clear diazonium salt solution was added to 600 cc. of cold 30% hypophosphorous acid and the mixture was allowed to stand three days at 5°, then three days at room temperature. The oil which separated was collected and the aqueous solution was extracted with 500 cc. of ether. The oil and ether solution were combined and washed with dilute sodium hydroxide and water. The oil remaining after removal of the ether was distilled from a modified Claisen flask. The fraction boiling at 115–119° (17 mm.) weighed 50 g. (70%).

Anal. Calcd. for $C_{10}H_{13}Br$: C, 56.5; H, 6.10. Found: C, 56.7; H, 6.19.

6. **Preparation of 3,5-Diethylbenzonitrile.**—A mixture of 30 g. of 3,5-diethylbromobenzene, 18 g. of anhydrous cuprous cyanide and 20 cc. of dry pyridine, in a flask with a ground glass joint connected to a reflux condenser, was heated in an oil-bath at 235–240° for sixteen hours. The mixture was cooled to 100° and added to a mixture of 75 cc. of water and 75 cc. of concentrated aqueous ammonia. The mixture was shaken with 110 cc. of benzene until the lumps were dispersed. Then 90 cc. of ether was added and the mixture was filtered. The organic layer was washed with dilute aqueous ammonia, dilute hydrochloric acid and saturated aqueous sodium chloride. Removal of the solvents and distillation of the residue gave 15 g. (67%) of 3,5-diethylbenzonitrile, b. p. 147.5–149° (29 mm.).

Anal. Calcd. for $C_{11}H_{13}N$: N, 8.82. Found: N, 8.82.

7. **Preparation of 3,5-Diethylbenzoic Acid.**—A mixture of 5 g. of sodium hydroxide, 50 cc. of ethylene glycol, 10 cc. of water and 10 g. of 3,5-diethylbenzonitrile was heated under reflux until ammonia was no longer evolved (four hours). The solution was diluted with 100 cc. of water and decolorized with norite. The filtrate was diluted to 500 cc. and acidified with 2% hydrochloric acid. The 3,5-diethylbenzoic acid, m. p. 128–129°, weighed 10.5 g. (94%). Recrystallization from 50% methanol gave 9.4 g. (85%) of material melting at 129.5–130°.

Summary

The oxidation of *sym*-triethylbenzene with dilute nitric acid produces small amounts of 3,5-diethylbenzoic acid, 3-aceto-5-ethylbenzoic acid, and 5-ethylisophthalic acid.

The reaction of bromobenzene, ethyl bromide, and aluminum chloride produces a mixture containing *p*-dibromobenzene and *sym*-triethylbenzene.

3,5-Diethylbenzoic acid may be prepared from commercial *m*-diethylbenzene by the following steps: nitration to 2,4-diethylnitrobenzene, reduction to 2,4-diethylaniline, bromination to 6-bromo-2,4-diethylaniline, deamination to 3,5-diethylbromobenzene, treatment with cuprous cyanide to give 3,5-diethylbenzonitrile, and hydrolysis to the acid.

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(10) Snyder and Shriner, *J. Chem. Ed.*, **17**, 588 (1940).

(11) Norris and Ingraham, THIS JOURNAL, **60**, 1421 (1938).

(12) Adams and Kornblum, *ibid.*, **63**, 194 (1941).