

Metalation of Phenyl 2-Thienyl Sulfone.—Thirty grams (0.134 mole) of phenyl 2-thienyl sulfone was treated with *n*-butyllithium prepared from 16.5 g. (0.179 mole) of *n*-butyl chloride and 2.6 g. (0.362 g. atom) of lithium. Nine grams of unreacted sulfone was recovered from the ether layer. The product, 2-benzenesulfonyl-5-thiophenecarboxylic acid, was recrystallized from a 50–50 mixture of ethanol and water; m.p. 205–207.5° (uncor.); weight 15 g.; conversion 41.6%, yield 60%. The m.p. was not lowered when mixed with an authentic sample prepared as outlined below.

Anal. Calcd. for $C_{11}H_8O_4S_2$: C, 49.25; H, 2.98. Found: C, 49.55; H, 3.07.

Sodium 2-Methyl-5-thiophenesulfonate.—Forty grams (0.5 mole) of sulfur trioxide was distilled into 200 ml. of dry ethylene chloride. With the temperature below 15°, 42 g. (0.5 mole) of dry dioxane was added slowly. With the temperature below 20°, 49 g. (0.5 mole) of 2-methylthiophene was added. When the addition was complete, the ice-bath was removed and the mixture stirred for two hours. It was then poured into water and the water layer separated and neutralized with sodium hydroxide to a pH of 7 using hydron paper as the indicator. The aqueous layer was evaporated and the solid obtained was extracted with hot 95% ethanol. On cooling the alcohol, the product separated; yield 49.2 g. (49.2%).

Two grams of sodium 2-methyl-5-thiophenesulfonate was heated for three hours on a steam-bath with 4 g. of phosphorus pentachloride. The mixture was poured on ice and an oily layer separated. Five milliliters of liquid ammonia was added to the oil. The resulting solid, 2-methyl-5-thiophenesulfonamide, after recrystallization from 95% ethanol, melted at 119.5–121°.

Anal. Calcd. for $C_8H_7O_2NS_2$: N, 7.91. Found: N, 7.94.

2-Benzenesulfonyl-5-methylthiophene.—2-Methyl-5-thiophenesulfonyl chloride (41.8 g., 0.212 mole), prepared by treating sodium 2-methyl-5-thiophenesulfonate with phosphorus pentachloride, was treated with 75 ml. of benzene and 28.5 g. of aluminum chloride. The product was recrystallized from 95% ethanol; m.p. 91–92.5°, yield 26 g. (51.4%).

Anal. Calcd. for $C_{11}H_{10}O_2S_2$: C, 55.46; H, 4.20. Found: C, 55.50; H, 4.20.

2-Benzenesulfonyl-5-thiophenecarboxylic Acid.—This was prepared from 2-benzenesulfonyl-5-methylthiophene following the oxidation procedure of Newell.¹³ The product was recrystallized from a 50–50 ethanol–water mixture and melted at 204–207° (uncor.).

Action of Lithium on the Bromophenyl Phenyl Sulfones.—One gram of lithium and 10 g. of *o*-bromophenyl phenyl sulfone were refluxed in ether under a dry nitrogen atmosphere for ten hours. Excess Dry Ice was then added. The mixture was hydrolyzed with dilute acid. The ether layer was extracted with 5% sodium hydroxide and evaporated. A quantitative recovery of unreacted sulfone was made. Acidification of the basic extract yielded no acidic material. The same results were obtained with *m*- and *p*-bromophenyl phenyl sulfones.

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Stobbe Condensation with Methyl γ -Benzoylbutyrate

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The Stobbe condensation with methyl γ -benzoylbutyrate gives a cyclized product Ia, together with a product of the normal type. Both substances are utilized to prepare the ester III, a valuable intermediate for steroid synthesis.

Recently, the Stobbe condensation with methyl γ -anisoylbutyrate was shown to produce both cyclized and normal products.¹ The cyclized half-ester (Ia) from methyl γ -benzoylbutyrate was obtained as a liquid in about 15% yield. It was purified by distillation of its methyl ester, which was obtained by the mild esterification procedure of Freudenberg and Jakob.² Hydrolysis of this gave a liquid acid, which was esterified with diazomethane to give the crystalline ester Ib. The structure of this substance, except for the position of the double-bond, was shown by its cyclization with sulfuric acid to 9-hydroxy-1-keto-1,2,3,4-tetrahydrophenanthrene, identified as its methyl ether IIa by comparison with an authentic sample.³

The position of the double-bond indicated in the structures Ia and Ib is supported by the absorption spectra, which show maxima at positions to be expected from the data for the cyclized ester from methyl γ -anisoylbutyrate (see Table II of the earlier paper).¹

The dimethyl ester Ic was converted to the homologous reduced ester III by methods employed previously.¹ The structure of this ester is demonstrated below.

The crude cyclic product from the Stobbe condensation was also reduced by the Raney alloy procedure⁴ to give a lactone acid presumed to be IV.

After the separation of the cyclic half-ester from the products of the Stobbe condensation, the normal Stobbe product was isolated as the unsaturated tricarboxylic acid V. The position of the double-bond in this acid was demonstrated by oxidation to γ -benzoylbutyric acid,⁵ using a procedure of Johnson and Hunt.⁶

The unsaturated acid was converted to a crystalline dimethyl ester; the trimethyl ester was a liquid. The nature of the dimethyl ester can be deduced from the known difficulty of esterifying α,β -unsaturated acids.⁷ It was reduced and cyclized to a product which should therefore be VI. The substance obtained from this by hydrogenolysis of the carbonyl group did not give recognizable

(4) E. Schwenk, D. Papa and B. Whitman, *J. Org. Chem.*, **7**, 587 (1942); E. Schwenk, D. Papa, B. Whitman and H. F. Ginsberg, *ibid.*, **9**, 175 (1944).

(5) The ultraviolet absorption spectrum of V, (λ_{max} , 237 m μ , $\log \epsilon$ 3.92) and that of the similar acid of W. S. Johnson, A. R. Jones and W. P. Schneider, *THIS JOURNAL*, **72**, 2395 (1950), (λ_{max} , 259 m μ , $\log \epsilon$ 3.85), determined in 95% ethanol, differ from the absorption of cinnamic acid, probably as a result of steric inhibition of resonance. Cf. Y. Hirschberg, *THIS JOURNAL*, **71**, 3241 (1949), and P. Ramart-Lucas, *Bull. soc. chim.*, **9**, 850 (1942).

(6) W. S. Johnson and R. H. Hunt, *THIS JOURNAL*, **72**, 935 (1950).

(7) E. N. Eccott and R. P. Linstead, *J. Chem. Soc.*, 2153 (1929).

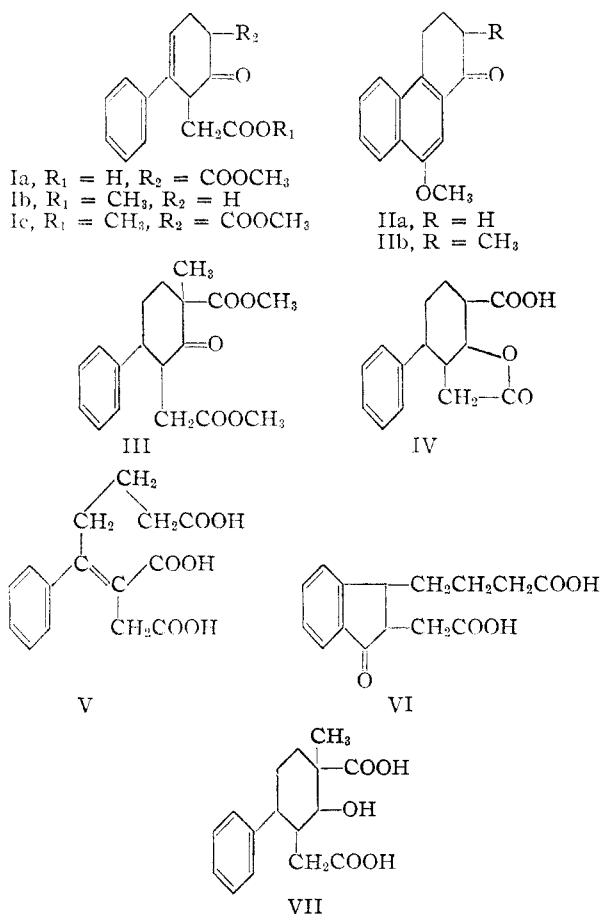
(1) D. L. Turner, *THIS JOURNAL*, **73**, 1284 (1951).

(2) K. Freudenberg and W. Jakob, *Ber.*, **74**, 1001 (1941).

(3) W. E. Bachmann and D. W. Holmes, *THIS JOURNAL*, **62**, 2750 (1940).

products on dehydrogenation. This supports the indene rather than the alternative tetrahydronaphthalene structure.

The double-bond in the unsaturated acid was reduced by the Raney alloy procedure⁴ and the resulting β -carboxy- γ -phenylsuberic acid was obtained crystalline with some difficulty. The trimethyl ester of this acid was submitted to Dieckmann cyclization, followed by methylation; this gave the crystalline ketoester III, obtained previously from Ia.⁸ The keto-ester III when pure, does not cyclize in the presence of sulfuric acid. It was brominated by the method of Ziegler⁹ and the product was treated with pyridine to remove hydrogen bromide. The object of preparing an α,β -unsaturated ketone in pure form was not achieved. The non-crystalline product was treated with sulfuric acid to give a cyclic phenol. The methyl ether of this phenol (IIb) was identified by comparison with an authentic sample.³ This transformation establishes the structure of the keto-ester III. The keto-ester was also hydrogenated and hydrolyzed to a crystalline product believed to be the hydroxy-acid VII.



This work was aided by a grant from the American Cancer Society recommended by the Com-

(8) J. Dutta and D. K. Banerjee, *Science and Culture*, **12**, 408 (1946), have reported dimethyl β -carbomethoxy- γ -phenylsuberate prepared by a different method. They also converted it to III but their product was a liquid and gave a rather unsatisfactory analysis.

(9) As modified by H. Schmid and P. Karrer, *Helv. Chim. Acta*, **29**, 573 (1946).

mittee on Growth of the National Research Council. I wish to thank Mrs. R. P. Gerhart and Miss Ruth Horcher for assistance. The microanalyses were performed by James Rigas, Brooklyn, N. Y., and Dr. E. W. D. Huffman, Denver, Colo.

Experimental^{10,11}

Stobbe Condensation with Methyl γ -Benzoylbutyrate.—To a refluxing solution of 100 g. of potassium in 2600 ml. of dry *t*-butyl alcohol under an atmosphere of nitrogen was added a mixture of 390 g. of methyl γ -benzoylbutyrate and 510 g. of dimethyl succinate. The mixture was refluxed under nitrogen for 45 minutes. A solid potassium salt separated during the course of the reaction. The mixture was cooled in nitrogen and the potassium salt was filtered and washed with a little *t*-butyl alcohol. Suction was applied using a rubber sheet¹² until the solid was dry. The potassium salt was dissolved in 2 l. of water and the solution was acidified with concentrated hydrochloric acid. The precipitated oil was taken up in ether, the ether was washed with saturated sodium chloride, dried over sodium sulfate and the solvent was removed to give an oil (A) weighing 211 g. (15% yield).

The *t*-butyl alcohol mother liquor was added gradually to an excess of 10% hydrochloric acid at about 0° and the precipitated oil was taken up in ether. Water was added to separate the layers. The extract was washed with water, and the acid product was taken out with 5% potassium carbonate. The alkaline solution was acidified with hydrochloric acid at about 5° and the precipitated oil was extracted with ether. The ethereal solution was washed with saturated sodium chloride and dried; the solvent was distilled to give 390 g. of oily half-ester (B) (64% yield).

In earlier experiments no attempt was made to separate the insoluble potassium salt mentioned above. For example, 69 g. of ethyl γ -benzoylbutyrate and 54.5 g. of ethyl succinate were refluxed with a solution of 12.2 g. of potassium in 320 ml. of dry *t*-butyl alcohol and the product, including the insoluble salt, was isolated as described for B above to give 79 g. of half-ester (C).

Methyl 3-Carbomethoxy-2-keto-6-phenyl-5-cyclohexen-1-acetate.—The product A above (211 g.) was dissolved in 500 ml. of methanol. The solution was cooled and treated with 100 ml. of acetyl chloride. After standing overnight, the mixture was evaporated *in vacuo* on the steam-bath and the residue was taken up in ether and washed with saturated sodium bicarbonate. The ethereal solution was dried over sodium sulfate, the solvent was removed and the residue was distilled at approximately 1 mm. A fraction I, b.p. 170–190° (37 g.), was collected and a fraction II, b.p. 190–200° (115 g.). Fraction II, redistilled at the same pressure, boiled nearly entirely at 198–200°, n_D^{20} 1.5357. The absorption spectrum showed a broad band with its center at about 260 $m\mu$ ($\log \epsilon$ 3.8).

Anal. Calcd. for $\text{C}_{17}\text{H}_{18}\text{O}_5$: C, 67.54; H, 6.00. Found: C, 66.78; H, 6.22.

Methyl 2-Keto-6-phenyl-5-cyclohexen-1-acetate (a) from Fraction I of the Preceding Distillation.—Fraction I of the preceding material was crystallized from ether by cooling in a Dry Ice-alcohol-bath and gave material, m.p. 77–78° (yield 2.1 g.). The absorption spectrum showed a broad band with its center at 262 $m\mu$ ($\log \epsilon$ 4.0).

Anal. Calcd. for $\text{C}_{16}\text{H}_{16}\text{O}_4$: C, 73.75; H, 6.60. Found: C, 73.89, 73.73; H, 6.70, 6.61.

The 2,4-dinitrophenylhydrazones of this ester was made in the usual manner and crystallized from a mixture of ethyl acetate and ethanol, m.p. 174°.

Anal. Calcd. for $\text{C}_{21}\text{H}_{20}\text{N}_4\text{O}_8$: C, 59.43; H, 4.75. Found: C, 59.80; H, 4.82.

(b) From Fraction II of the Preceding Distillation.—The dimethyl ester from fraction II (5.0 g.) was dissolved in 25 ml. of ethanol and treated with 10 ml. of 45% potassium hydroxide solution. The mixture was refluxed for 1 hour,

(10) The absorption spectra were determined with the Beckman quartz spectrophotometer, using 95% ethanol as solvent.

(11) The dry solvents were dried over calcium hydride obtained from Metal Hydrides, Inc., Beverly, Mass.

(12) L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 321.

diluted with water, acidified with hydrochloric acid and extracted with ether. The ethereal solution was mixed with an excess of ethereal diazomethane and the solvent was evaporated. The ester was crystallized from ether, in which it is quite soluble, to give 1.0 g. of pure ester, m.p. 77–78° alone or when mixed with the ester from fraction I. Additional material was present in the nearly completely crystalline mother liquor.

2,4-Dinitrophenylhydrazone of 2-Keto-6-phenyl-5-cyclohexen-1-acetic Acid.—The preceding crystalline ester (1.0 g.) was refluxed for 30 minutes in 10 ml. of ethanol with 1.0 ml. of 45% potassium hydroxide solution. The solution was diluted with water, acidified and extracted with ether. The ethereal solution was dried, the solvent was removed and the oily residue was converted to the 2,4-dinitrophenylhydrazone. This was crystallized from ethyl acetate to give 1.1 g., decomposing at 239°, when inserted at 225°.

Anal. Calcd. for $C_{20}H_{18}O_6N_4$: C, 58.53; H, 4.42. Found: C, 58.61; H, 4.39.

1-Keto-9-methoxy-1,2,3,4-tetrahydrophenanthrene.—To 0.5 g. of methyl 2-keto-6-phenyl-5-cyclohexen-1-acetate was added 10 ml. of sulfuric acid. The mixture was heated on the steam-bath for 12 minutes. It was then poured into water and filtered. The solid product was methylated by dissolving in 10 ml. of 10% sodium hydroxide solution and heating on the steam-bath with 1 ml. of methyl *p*-toluenesulfonate¹³ for 1 hour. An additional 10 ml. of 10% sodium hydroxide was added and heating was continued for an additional hour. The product was cooled, the precipitated crystals were filtered and recrystallized from methanol to give 0.16 g. (35% yield), m.p. 97–98° alone or when mixed with an authentic sample of 1-keto-9-methoxy-1,2,3,4-tetrahydrophenanthrene (m.p. 97–98°) prepared according to Bachmann and Holmes.³

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.73; H, 6.32.

Reduction of the Crude Stobbe Product A.—To 20 g. of the crude Stobbe product A was added 600 ml. of 10% sodium hydroxide solution. The solution was heated on the steam-bath with stirring, while 60 g. of Raney nickel-aluminum alloy was added during 1 hour. The mixture was heated and stirred for an additional hour. It was filtered, cooled and acidified with enough hydrochloric acid to dissolve the precipitated aluminum salts. It was saturated with sodium chloride and extracted 3 times with ether. The ethereal extract was washed and dried, the solvent was distilled and the residual oil was crystallized repeatedly from ethyl acetate to give 1.7 g., m.p. 228–230°. This is presumed to be 3-carboxy-2-hydroxy-6-phenylcyclohexan-1-acetic acid γ -lactone.

Anal. Calcd. for $C_{15}H_{16}O_4$: C, 69.20; H, 6.20; neut. equiv., 260; mol. wt., 260. Found: C, 69.44; H, 6.25; neut. equiv., 258.5; mol. wt. (Rast), 258.0.

The methyl ester lactone was made with ethereal diazomethane and crystallized from ether-pentane, m.p. 91–92°.

Anal. Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.20, 70.11; H, 6.62, 6.65.

3-Phenyl-2-hexene-1,2,6-tricarboxylic Acid.—To 13 g. of the crude Stobbe condensation product B or C was added 90 ml. of ethanol and a solution of 20 g. of barium hydroxide octahydrate in 150 ml. of water. The mixture was refluxed for 1 hour; it was cooled, filtered, and the solid barium salts were decomposed with concentrated hydrochloric acid. After dilution with water, and cooling, the acid crystallized. It was recrystallized from ethyl acetate, containing benzene, and then from ethyl acetate alone, m.p. 154–154.5°. The yield was 3.3 g. from C and 5.4 g. from B.

Anal. Calcd. for $C_{18}H_{16}O_6$: C, 61.63; H, 5.52; neut. equiv., 97.4. Found: C, 61.45; H, 5.58; neut. equiv., 98.2.

By repeated recrystallization of a sample a m.p. of 162–164° was obtained. The lower m.p. was observed when this was mixed with the preceding; λ_{max} . 237 $m\mu$ (log ϵ 3.92).

Anal. Calcd. for $C_{18}H_{16}O_6$: C, 61.63; H, 5.52. Found: C, 61.86; H, 5.64.

Oxidation of the Unsaturated Acid to γ -Benzoylbutyric Acid.—A solution of the preceding acid (3 g., m.p. 154–154.5°) in 300 ml. of acetone (distilled from potassium permanganate) was cooled to 0° and 10 g. of finely powdered potassium permanganate was added gradually. There was no apparent reaction at the low temperature. The mixture was warmed to 25° and stirred for 4 hours. The acetone was evaporated in a current of air, without heating. To the residue was added 200 ml. of water, 100 ml. of 4 *N* sulfuric acid and 70 ml. of saturated sodium bisulfite solution. The decolorized solution was saturated with sodium chloride and extracted thoroughly with ether. Acidic material was removed from the ether with saturated sodium bicarbonate and this solution was acidified with 4 *N* sulfuric acid. The crystals that separated were filtered, and recrystallized from ethanol giving 0.52 g., m.p. 123–124.5°, alone or when mixed with an authentic sample of γ -benzoylbutyric acid.

Anal. Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.30. Found: C, 68.67; H, 6.26.

Dimethyl Ester of the Unsaturated Acid.—A suspension of 5 g. of the tricarboxylic acid (m.p. 154–154.5°) in 165 ml. of ethylene dichloride was treated with 2.0 ml. of methanol and 4.0 ml. of acetyl chloride.² The mixture was refluxed for two hours, but the acid did not dissolve. To the hot solution was added 100 ml. of methanol and 5 ml. of acetyl chloride. A clear solution was obtained, which was allowed to stand without heating for 1 hour. The solution was diluted with water; the ethylene chloride layer was separated and extracted with saturated sodium bicarbonate solution. The alkaline solution was acidified with hydrochloric acid, and the precipitated acid was taken up in ether. The ethereal solution was washed, dried and distilled to remove solvent. The residue was crystallized from ether-pentane to give 1.5 g., m.p. 81–83°. Recrystallized from ethane-pentane, it melted at 83–85°; λ_{max} . 237 $m\mu$ (log ϵ 3.80).

Anal. Calcd. for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29; neut. equiv., 320.3; sapn. equiv., 106.7. Found: C, 63.47; H, 6.40; neut. equiv., 303.7; sapn. equiv., 107.0.

Hydrolysis of the ester-acid gave the original tricarboxylic acid.

Cyclization of the Dimethyl Ester.—The preceding dimethyl ester (10 g.) was hydrogenated in methanol using 5 g. of palladium on Darco G-60 containing 5% palladium,¹⁴ at a pressure of 60 p.s.i. After the theoretical amount of hydrogen was absorbed, the mixture was filtered and the solvent was evaporated. The residue was suspended in 50 ml. of dry ether containing 4 drops of pyridine. The mixture was cooled in an ice-hydrochloric acid-bath and treated with 7 ml. of thionyl chloride.¹⁵ After the acid had dissolved, the mixture was allowed to stand at 25° for 30 minutes. The solvent was removed *in vacuo*. Dry thiophene-free benzene was added and the solvent and thionyl chloride were again removed at a temperature below 50° *in vacuo*. The residue was dissolved in 60 ml. of dry benzene, the solution was cooled to 5° and 15 ml. of stannic chloride in 15 ml. of benzene was added. After swirling for 10 minutes, the mixture was hydrolyzed with ice and hydrochloric acid and extracted with ether. The ethereal solution was washed with 10% hydrochloric acid, saturated sodium bicarbonate, and dried. The ether was removed and the residue was hydrolyzed by refluxing with 50 ml. of methanol and 10 ml. of 45% potassium hydroxide solution for 30 minutes. The solution was diluted with 50 ml. of water, the methanol was distilled, and the residue was cooled and acidified. The product was taken up in ether and isolated in the usual manner. Crystallized from ethyl acetate, it weighed 0.5 g., m.p. 176–178°. This is presumed to be 2-carboxymethyl-1-indanone-3-butyric acid.

The absorption spectrum showed maxima at 292 $m\mu$ (log ϵ 3.30) and 251 $m\mu$ (4.14), and a minimum at 275 $m\mu$ (3.12). This is essentially the spectrum of 1-tetralone but the spectrum of indanone is not sufficiently different for this observation to be significant.¹⁶

Anal. Calcd. for $C_{15}H_{16}O_5$: C, 65.20; H, 5.84. Found: C, 65.40; H, 5.86.

Reduction of the Preceding Acid.—A solution of the preceding acid (400 mg.) in 25 ml. of acetic acid was hydro-

(13) A. Cohen, J. W. Cook and C. L. Hewett, *J. Chem. Soc.*, 445 (1935).

(14) R. Mazingo, *Org. Syntheses*, **26**, 77 (1946), method B.

(15) Purified by the method of L. F. Fieser, ref. 12, p. 381.

(16) D. Biquard, *Bull. soc. chim.*, **8**, 55 (1941).

generated at 50 p.s.i. in the presence of 0.2 g. 30% palladium-on-Darco G-60¹⁷ and 2 ml. of 60% perchloric acid.¹⁸ After 2 hours, the mixture was filtered and the solution was diluted with water and extracted with ether. The ethereal solution was washed with water until it was free of acetic acid; it was dried and the solvent was evaporated. The residue was crystallized from ether, m.p. 156–157.5°. This is presumed to be 2-carboxymethyl-indane-3-butyric acid.

Anal. Calcd. for C₁₅H₁₈O₄: C, 68.68; H, 6.92. Found: C, 68.77; H, 6.96.

β -Carboxy- γ -phenylsuberic Acid (a) from the Pure 3-Phenyl-2-hexene-1,2,6-tricarboxylic Acid.—The unsaturated acid (1.3 g., m.p. 154–154.5°) was dissolved in 85 ml. of 10% sodium hydroxide solution. The solution was heated on the steam-bath and stirred vigorously, while 10 g. Raney nickel–aluminum alloy was added during the course of one hour. The mixture was heated and stirred for an additional hour. It was filtered, cooled and acidified with sufficient concentrated hydrochloric acid to dissolve all of the aluminum salt that first precipitated. The mixture was then saturated with sodium chloride, cooled again, and extracted ten times with ether. Thorough extraction is necessary because the product is very soluble in water. The ether was washed with saturated sodium chloride solution, and dried over sodium sulfate. The ether was removed by distillation, and benzene was added and distilled from the residue until the product was dry. The benzene solution gave crystals on cooling (1.1 g., m.p. 83–97°). The crystalline substance contained solvent of crystallization, which was expelled by dissolving in boiling water and allowing the benzene to distil in steam. The substance will not crystallize from water in the presence of a trace of benzene. The cooled aqueous solution gave crystals after standing for 1 week. The substance was crystallized twice from water to give 0.79 g., m.p. 148–150°; mixed with the unsaturated acid (m.p. 154–154.5°), the m.p. was 128–139°. This reduction was carried out successfully in batches of 25 g. in 1 liter of 10% sodium hydroxide with 120 g. of Raney alloy. The yield was diminished, 8 g. of pure product being obtained.

Anal. Calcd. for C₁₈H₁₈O₆: C, 61.21; H, 6.16; neut. equiv., 98.1. Found: C, 61.30; H, 6.35; neut. equiv., 99.0.

The trimethyl ester prepared by the method of Clinton and Laskowski¹⁹ was a liquid, b.p. 185° (1–1.5 mm.), n_D^{20} 1.4910.

(b) **From the Crude Stobbe Product C.**—A solution of C (80 g.) in 160 ml. of methanol containing 2 ml. of acetic acid, was hydrogenated over 1.5 g. of Adams platinum oxide catalyst at 3 atm. The uptake of hydrogen soon ceased, and it was necessary to add fresh catalyst several times before the theoretical amount of hydrogen was absorbed. The oily product remaining after evaporation of the solvent was hydrolyzed by refluxing for 1 hour with a solution of 60 g. of potassium hydroxide in 25 ml. of water and 100 ml. of ethanol. The product was diluted with water, and extracted with ether. The aqueous solution was acidified and extracted with ether. The product was isolated in the usual manner and dried by distilling benzene from it. This gave 34 g. of crystals containing benzene, m.p. 93–102°. Crystallized several times from benzene the substance melted at 103–105°; crystallized from anisole the m.p. was 125–127°. When dried *in vacuo* at 65° the substance became a glass, which could be converted to the original crystals by rubbing with the appropriate solvent. The glass obtained by drying crystals from benzene was analyzed.

Anal. Calcd. for C₁₅H₁₈O₆· $\frac{1}{2}$ C₆H₆: C, 63.74; H, 6.29. Found: C, 63.78; H, 6.15.

Crystallization from water as in (a) gave material m.p., alone or when mixed with the acid of (a), 148–150°.

β -Carboxy- γ -cyclohexylsuberic Acid.—The preceding acid as the benzene compound from (b) (5 g.) was hydrogenated in 500 ml. of ethyl acetate over 1 g. of Adams catalyst at 3 atm. pressure. Evaporation of the solvent gave 1.2 g., m.p. 191–193° after recrystallization from ethyl acetate.

Anal. Calcd. for C₁₆H₂₄O₆: C, 59.98; H, 8.05; neut.

(17) Prepared by Method B of Mzingo, ref. 14, with an increased amount of palladium chloride.

(18) K. W. Rosenmund and E. Karg, *Ber.*, **75**, 1850 (1942).

(19) R. O. Clinton and S. Laskowski, *THIS JOURNAL*, **70**, 3135 (1948).

equiv., 100.1. Found: C, 59.82; H, 8.07; neut. equiv., 102.8.

Methyl 3-Carbomethoxy-2-keto-3-methyl-6-phenylcyclohexan-1-acetate (a) from the Liquid Methyl 3-Carbomethoxy-2-keto-6-phenyl-5-cyclohexen-1-acetate.—A solution of 22 g. of fraction II of the distilled ester described above in 250 ml. of methanol was mixed with 10 g. of 2% palladium-on-strontium carbonate^{20,21} and hydrogenated at 59 p.s.i. at 40°. After 20 minutes, the theoretical amount of hydrogen was absorbed. The mixture was filtered and the solvent was evaporated. The residue was dried by distilling benzene from it. It was dissolved in 200 ml. of dry benzene and refluxed with a solution of 4.6 g. of sodium in 100 ml. of dry methanol for 10 minutes. The mixture was cooled in ice-water and treated with 20 ml. of methyl iodide. After standing overnight at room temperature, it was treated with an additional 20 ml. of methyl iodide and refluxed for 1 hour. The mixture was cooled, acidified with acetic acid, and evaporated *in vacuo*. The residue was taken up in benzene, and the solution was washed with water, sodium thiosulfate solution, and saturated sodium bicarbonate. The benzene solution was dried and the solvent was evaporated. The residue was crystallized from methanol to give 4.4 g., m.p. 111°, alone or when mixed with the preparations of (b) and (c).

Anal. Calcd. for C₁₈H₂₂O₅: C, 67.90; H, 6.97. Found: C, 67.98, 68.13; H, 6.97, 7.09.

(b) **From Pure β -Carboxy- γ -phenylsuberic Acid.**—The acid, m.p. 148–150° (5 g.) was esterified with diazomethane in ether. The ester was dried by distilling benzene from it. It was dissolved in 100 ml. of benzene and added to dry sodium methylate prepared by dissolving 0.8 g. of sodium in 100 ml. of methanol and distilling *in vacuo* at 100°. The mixture was refluxed for 4 hours under nitrogen. It was cooled to room temperature and treated with 10 ml. of methyl iodide. After standing overnight, an additional 10 ml. of methyl iodide was added and the mixture was refluxed for 2 hours. The subsequent treatment followed (a) above. The product from ethanol gave large prisms, m.p. 111°, alone or when mixed with the product of (a) or (c).

Anal. Calcd. for C₁₈H₂₂O₅: C, 67.90; H, 6.97. Found: C, 67.95, 67.87; H, 6.98, 7.05.

(c) **From the Stobbe Product C.**—Seventy-nine grams of Stobbe half-ester C was converted to crude β -carboxy- γ -phenylsuberic acid as described above without attempting to crystallize the acid. The 51 g. of acid, obtained as an oil was directly esterified by the method of Clinton and Laskowski.¹⁹ The dimethyl β -carbomethoxy- γ -phenylsuberate boiled at 180° (1 mm.), n_D^{20} 1.4948, and weighed 26 g.

Anal. Calcd. for C₁₈H₂₄O₆: C, 64.27; H, 7.19. Found: C, 64.97; H, 7.30.

To a solution of 67.6 g. of ester prepared in this manner in 400 ml. of dry benzene, was added 23 g. of dry sodium methylate (obtained from the Mathieson Chemical Corp.). The solution was refluxed under nitrogen for two hours. It was then cooled and treated with 50 ml. of methyl iodide and 100 ml. of dry methanol. After standing overnight, 20 ml. of methyl iodide was added and the mixture was refluxed for 1 hour. The subsequent treatment followed (a) above. The product from ethanol, m.p. 109–110°, weighed 23 g. A sample was recrystallized three times from ethanol, m.p. 111° alone or when mixed with material from (a) or (b).

Anal. Calcd. for C₁₈H₂₂O₅: C, 67.90; H, 6.97. Found: C, 67.67; H, 6.76.

1-Keto-9-methoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene.—To 3.18 g. of the preceding cyclic ester made by method (b), m.p. 111°, was added 100 mg. of benzoyl peroxide, 1.78 g. of N-bromosuccinimide and 100 ml. of carbon tetrachloride. After refluxing for 2 hours, the mixture was cooled and filtered. The carbon tetrachloride solution was washed with saturated sodium bicarbonate, dried, and distilled *in vacuo*. To the residue was added 20 ml. of dry pyridine and the solution was refluxed for 4 hours. It was diluted with water and extracted thoroughly with ether. The ethereal solution was washed with 2 N hydrochloric acid and water and dried. The solvent was removed by distillation. The residue gave 1.0 g. of the starting material when crystallized from methanol. The methanol was evaporated

(20) A. Koebner and R. Robinson, *J. Chem. Soc.*, 1994 (1938).

(21) W. S. Johnson and H. Posvic, *THIS JOURNAL*, **69**, 1361 (1947).

from the mother liquor to give an oil. This was dissolved in 4 ml. of concentrated sulfuric acid and heated on the steam-bath for 5 minutes. It was poured on ice and extracted 5 times with ether. The ethereal solution was washed with saturated sodium chloride and dried. The solvent was distilled. The residue was dissolved in 10 ml. of 10% sodium hydroxide and methylated in the usual way with methyl *p*-toluenesulfonate.¹³ The product was crystallized from methanol to give 0.25 g. of yellow crystals, m.p. 84–86°, alone or when mixed with an authentic sample of 1-keto-2-methyl-9-methoxy-1,2,3,4-tetrahydrophenanthrene.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.97; H, 6.71. Found: C, 79.96, 80.07; H, 6.64, 6.70.

Pure samples of the crystalline cyclic keto-ester hydrolyzed with alcoholic potash and then treated with sulfuric acid or

treated with sulfuric acid directly did not cyclize to the tetrahydrophenanthrene.

3-Carboxy-2-hydroxy-3-methyl-6-phenylcyclohexan-1-acetic Acid.—The cyclic keto-ester (III, 1.0 g.) was hydrogenated in 100 ml. of ether with 1.0 g. of Adams platinum oxide catalyst at 3 atm. The product was hydrolyzed in 30 ml. of methanol and 2.5 ml. of 45% potassium hydroxide by refluxing for 30 minutes. The solution was filtered, diluted with water, acidified and extracted with ether. After the usual treatment, the product was crystallized from ethyl acetate, m.p. 163–165° (dec.).

Anal. Calcd. for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.90; H, 6.88.

PHILADELPHIA, PENNA.

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(22) Original manuscript received April 14, 1950.

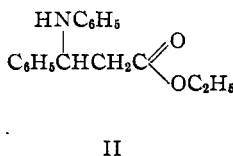
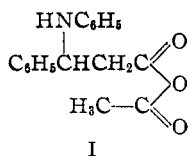
[CONTRIBUTION FROM THE MALLINCKRODT CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Action of Acetic Anhydride on Benzalaniline. A Reinvestigation

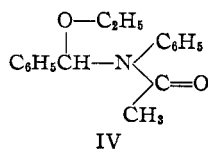
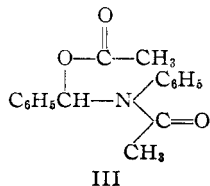
BY ALBERT W. BURGSTAHLER¹

It is verified that the reaction of acetic anhydride with benzalaniline leads to the formation of *N*-(α -acetoxybenzyl)-acetanilide (III), which ethanol converts to *N*-(α -ethoxybenzyl)-acetanilide (IV). Both of these products yield *N*-ethyl-*N*-phenylbenzylamine when reduced with lithium aluminum hydride.

Recently it has been proposed² that the previously observed³ product formed by the action of acetic anhydride on benzalaniline under mildly acidic conditions is acetic β -anilinohydrocinnamic anhydride (I), postulated to arise as the first-stage of a Perkin type addition of acetic anhydride to the $>C=N-$ system in benzalaniline. Among the considerations adduced in support of this view were: (i) the nearly quantitative reversion of the product to benzalaniline and acetic anhydride on heating, or to benzaldehyde and acetanilide (or aniline) under acidic hydrolytic conditions; (ii) the ready reaction of the adduct with ethanol to form an ethoxy derivative, considered to be ethyl β -anilinohydrocinnamate (II); and (iii) the conversion of the adduct to ethyl cinnamate (or cinnamic acid) on treating with sodium ethoxide.



All of these transformations, however, are in accord with those which might be anticipated from the isomeric formulation III, proposed earlier by Ekeley, *et al.*^{3b} Thus, *N*-(α -acetoxybenzyl)-



acetanilide (III), is a structure closely related to an acetal and should therefore be easily convertible with aqueous acid to the parent aldehyde (benzaldehyde), acetic acid and acetanilide, as observed.² The reformation of benzalaniline and acetic anhydride on heating is also readily explicable in terms of formula III. Moreover, the formation of an ethoxy derivative by reaction with ethanol, rather than necessarily indicating the presence of an anhydride system in the adduct, is interpretable on the basis of III as a solvolytic cleavage by the alcohol present in excess, leading to *N*-(α -ethoxybenzyl)-acetanilide (IV) and acetic acid.⁴ This product (IV), like III, would be expected to undergo the observed² facile reversion to benzaldehyde and acetanilide when treated with acid. Lastly, the reaction of the addition product with excess sodium ethoxide to form ethyl cinnamate (or cinnamic acid) along with acetanilide and a small amount of benzaldehyde and aniline, is a foreseeable result on the basis of formula III through the intermediate generation of benzaldehyde and ethyl acetate, which then react by a normal Claisen condensation in the presence of the strong base to yield ethyl cinnamate and thence cinnamic acid by partial hydrolysis from the water formed in this latter reaction. Partial hydrolysis of the acetanilide produced accounts for the aniline observed.² The fact that benzaldehyde is also isolated² is further evidence in support of this interpretation.

In confirmation of these deductions, conclusive verification of structures III and IV for the respective products can now be reported. The infrared spectra of these compounds have been determined, and the following relevant features may be considered. The absence of any definite absorption in the $>N-H$ (or $-O-H$) region ($2.9-3.0\mu$) places the formulations I and II in immediate

(1) National Institute of Health Predoctoral Fellow, Harvard University, 1950–1951.

(2) H. S. Angel and A. R. Day, *THIS JOURNAL*, **72**, 3874 (1950).

(3) (a) M. Passerini and M. P. Macentelli, *Gazz. chim. ital.*, **58**, 641 (1928); (b) J. B. Ekeley, M. C. Swisher and C. C. Johnson, *ibid.*, **62**, 81 (1932); (c) H. R. Snyder, R. H. Levin and P. F. Wiley, *THIS JOURNAL*, **60**, 2025 (1938).

(4) The almost quantitative formation of acetic acid and not ethyl acetate in this reaction (*cf.* Experimental) is in agreement with this proposed mechanism and clearly indicates that the process is actually a solvolysis and not a simple ester exchange.