lysozyme which was used in these experiments in order to determine its purity and to acknowledge the work of Miss Lois M. Kay and Mr. Lewis Honnen in performing certain of the experiments reported here. The kindness of Dr. James R. Vaughan, Jr., in offering a sample of synthetic tetrapeptide is greatly appreciated. This work was aided by a grant from the National Foundation for Infantile Paralysis.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, UNIVERSITY OF WASHINGTON]

The Synthesis of 5,6,7,7a,8,9,10,11-Octahydro-4H-benzo[ef]heptalene[1]

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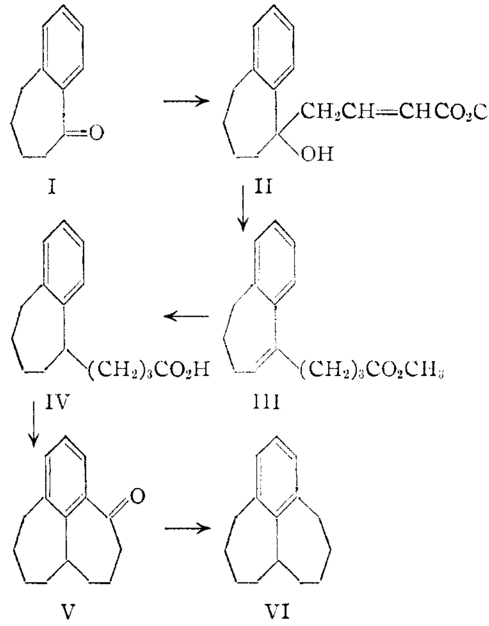
5,6,7,7a,8,9,10,11-Octahydro-4H-benzo[ef]heptalene, a hydrocarbon having a new tricyclic fused ring system, has been synthesized from 6,7,8,9-tetrahydro-5H-cycloheptabenzen-5-one.

In the course of investigations on the synthesis of hydrocarbons related to heptalene, pentalene or azulene which have new tricyclic fused rings systems, we have prepared 5,6,7,7a,8,9,10,11-octahydro-4H-benzo[ef]heptalene (VI). To our knowledge no compounds having this ring system have been reported previously. As the four other possible tricyclic systems containing five- and seven-membered rings fused to adjacent sides of a benzene ring[2] have been prepared previously,[3] the synthesis of VI completes this particular series of compounds.

A synthetic route to VI *via* 6,7,8,9-tetrahydro-5H-cycloheptabenzen-5-one (I) was selected and this intermediate was prepared in 89% yield by the cyclization of phenylvaleryl chloride in an inverse Friedel–Crafts reaction.



A Reformatsky reaction of I with methyl bromocrotonate gave a product (presumably II) which was unstable to heat and, accordingly, was subjected to catalytic hydrogenation without purification. The saturated product was also quite unstable and, similarly, was dehydrated without purification to give methyl 8,9-dihydro-7H-cycloheptabenzene-5-butyrate (III)[4] in 25% over-all yield from I. The observed instability of both the unsaturated and saturated hydroxy esters is in agreement with the results of Bachmann and coworkers[5] on similar compounds. The dehydration of the saturated hydroxy ester was unexpectedly difficult to accomplish. Heating the compound with anhydrous, fused potassium bisulfate at 150–160°[5] was the most satisfactory method found. The use of p-toluenesulfonic acid, β-naphthalenesulfonic acid, iodine or oxalic acid as catalysts gave over-all yields of 5% or less of III.

Saponification of III and catalytic hydrogenation of the acidic product, which was a viscous oil and unstable to heat, gave 6,7,8,9-tetrahydro-5H-cycloheptabenzene-5-butyric acid (IV) in 56% yield. A Friedel–Crafts cyclization of the acid chloride of IV afforded a 58% yield of 5,6,7,7a,8,9,10,11-octahydro-4H-benzo[ef]heptalen-4-one (V). A modified Wolff–Kishner reduction of V gave 5,6,7,7a,8,9,10,11-octahydro-4H-benzo[ef]heptalene in 38% yield. The structure of VI was shown by analysis and oxidation with potassium permanganate followed by esterification of the acidic product to give the known trimethyl hemimellitate.

Experimental[6]

Phenylvaleric Acid.—From 132 g. (1.0 mole) of cinnamaldehyde, 115 g. (1.1 moles) of malonic acid, 50 ml. of dry benzene and 13 ml. of 10% alcoholic potassium hydroxide was obtained, in a manner similar to that described by Welch,[7] 190 g. (83%) of cinnamylidenemalonic acid. The crude product melted at 198–202° and was used without further purification. A sample recrystallized from alcohol melted at 205–207° with decomposition.[8]

A solution of 109 g. (0.5 mole) of the crude cinnamylidenemalonic acid and 150 g. of sodium hydroxide in 1200 ml. of water was treated with Raney nickel catalyst powder[9] (100

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[1] From the Ph.D. Thesis of Helen Frances Greef.

[2] The structure of this type having two five-membered rings fused to the benzene ring would not appear to be possible.

[3] J. v. Braun and J. Reutter, *Ber.*, **59**, 1922 (1926); J. v. Braun and E. Roth, *ibid.*, **60**, 1182 (1927).

[4] The position of the double bond was not determined and it may be exocyclic to the seven-membered ring.

[5] W. E. Bachmann and N. L. Wendler, THIS JOURNAL, **68**, 2580 (1946); W. E. Bachmann and A. S. Dreiding, *J. Org. Chem.*, **13**, 317 (1948).

[6] Melting points and boiling points are uncorrected.

[7] K. N. Welch, *J. Chem. Soc.*, 673 (1931).

[8] B. S. Bansal and K. C. Pandya, *J. Indian Chem. Soc.*, **24**, 443 (1947).

[9] D. Papa, E. Schwenk and B. Whitman, *J. Org. Chem.*, **7**, 587 (1942).

g.) essentially as described by Cook, *et al.*[10] The yield of phenylpropylmalonic acid melting at 92–95° (reported 95°)[11] was 110 g. (99%), and from this material was obtained, after thermal decarboxylation at 170–180° under reduced pressure, 85 g. (94%) of phenylvaleric acid (m.p. 54–57°). Recrystallization of a sample from 60–90° ligroin raised the melting point to 58–59°.[12]

6,7,8,9-Tetrahydro-5H-cycloheptabenzen-5-one (I).—In accordance with the procedure of Plattner[13] as modified by Aspinall and Baker,[14] from 130 g. (0.87 mole) of phenylvaleryl chloride (prepared from 140 g. of phenylvaleric acid and 140 g. of thionyl chloride) and 176 g. of aluminum chloride was obtained 97 g. (89%) of the desired ketone as the fraction boiling at 134–136° at 11 mm. (or 99–102° at 1 mm.); n^{20}_{D} 1.5636.[13]

Methyl 8,9-Dihydro-7H-cycloheptabenzene-5-butyrate (III).—A Reformatsky reaction of 20 g. of zinc, 16 g. (0.10 mole) of the aforementioned tetrahydrocycloheptabenzenone and 18 g. of methyl bromocrotonate, then hydrogenation of the oily product containing II and, finally, dehydration of the reduced product by heating with potassium bisulfate were carried out as described by Bachmann, *et al.*,[5] for similar compounds. Final distillation gave 6 g. (25%) of III as a viscous, colorless oil (b.p. 120–122° at 0.2 mm.) which slowly became yellow on standing in air. The ultraviolet absorption spectrum of an ethanolic solution had a maximum at 243 mμ (ε 7200).

Anal. Calcd. for $C_{16}H_{20}O_2$: C, 78.65; H, 8.20. Found: C, 78.22; H, 7.94.

6,7,8,9-Tetrahydro-5H-cycloheptabenzene-5-butyric Acid (IV).—Saponification of III was performed by heating 24.4 g. (0.1 mole) of the ester under reflux with a solution of 22 g. of potassium hydroxide in 100 ml. of 50% ethanol for several hours. The crude acidic oil (18 g.) obtained from the reaction mixture was dissolved in 50 ml. of glacial acetic acid and hydrogenated in the presence of 1 g. of a reduced platinum oxide catalyst at 30–40 lb. pressure. Removal of the acetic acid left a dark oil which solidified on standing. Three recrystallizations from nitromethane (or acetonitrile) gave 16 g. (70%) of light tan crystals; m.p. 84–87°. Evaporative distillation of a sample (b.p. 135° at 0.2 mm.) afforded colorless crystals of IV melting at 87–88°.

Anal. Calcd. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.38; H, 8.78.

5,6,7,7a,8,9,10,11-Octahydro-4H-benzo[ef]heptalen-4-one (V).—Anhydrous benzene (43 ml.) was added dropwise to a mixture of 2.3 g. (0.01 mole) of the saturated acid (IV) and 2.3 g. (0.01 mole) of phosphorus pentachloride and the reaction mixture warmed (40–50°) for one hour. The solvent and volatile by-products were removed at 60–70° under reduced pressure and 30 ml. of dry benzene then added and the distillation repeated. This procedure was repeated three more times. The final residual oil containing the acid chloride was taken up in 300 ml. of carbon disulfide and this solution added slowly over a period of 90 minutes to a gently refluxing mixture of 300 ml. of carbon disulfide and 1.9 g. (0.014 mole) of anhydrous aluminum chloride. The mixture was then heated under reflux for six hours, the solvent removed and 200 g. of ice added to the residue. The mixture thus formed was extracted with ether and the extracts washed with dilute hydrochloric acid, saturated sodium bicarbonate and saturated sodium chloride solutions. After drying over sodium sulfate and removing the solvent, distillation gave 1.26 g. (58%) of ketonic product as a viscous pale yellow oil; b.p. 122–126° at 0.1 mm. An analytical sample was obtained by redistillation; b.p. 130° at 0.2 mm., n^{25}_{D} 1.5763.

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.05; H, 8.47. Found: C, 84.01; H, 8.51.

6,7,7a,8,9,10,11-Octahydro-4H-benzo[ef]heptalene (VI).—A mixture of 0.8 g. (0.004 mole) of the tricyclic ketone (V) and 2 g. of 85% hydrazine hydrate was refluxed vigorously for two hours. The cooled mixture was extracted several times with ether and the combined extracts dried over solid potassium hydroxide. To the yellow oil which remained after removal of the solvent was added 0.5 g. of solid potassium hydroxide and the mixture heated to 150–160° until the evolution of nitrogen had ceased (*ca.* one hour). After the addition of 25 ml. of water to the cooled mixture, it was extracted with ether and the ethereal solution washed with water and dried over sodium sulfate. Removal of the solvent followed by distillation under reduced pressure gave 0.3 g. (38%) of VI as a colorless liquid; b.p. 95–97° at 0.15 mm., n^{25}_{D} 1.5634.

Anal. Calcd. for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 90.14; H, 10.00.

Trimethyl Hemimellitate.—To a mixture of 1 g. (0.005 mole) of VI and 100 ml. of water heated to 100° was added a total of 13.5 g. (0.085 mole) of potassium permanganate in *ca.* 2-g. portions over a period of five days. The solution was allowed to become colorless each time before adding the next portion of the oxidizing agent. The solution was colorless on the sixth day and an additional gram of permanganate was added. On the seventh day the mixture was cooled, decolorized by the addition of a small amount of sodium bisulfite and filtered. The filtrate was concentrated to 25 ml., extracted with ether and then acidified and evaporated to dryness. The dry residue was powdered and extracted with ether in a soxhlet apparatus for several hours. The ethereal extracts were evaporated to dryness and the solid residue treated with an ethereal solution of diazomethane prepared from 5 g. of N-methyl-N-nitrosourea. After decantation from a small amount of unreacted material and the addition of acetic acid (dropwise until the solution became colorless), the solution was concentrated to *ca.* 15 ml. and allowed to cool. The colorless plates which separated amounted to 0.5 g. and an additional 0.2 g. was obtained from the filtrate to give a total yield of 0.7 g. (70%) of material which melted at 97–99°. Recrystallization from methanol raised the melting point to 100–101° in agreement with the value reported for trimethyl hemimellitate.[15]

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[10] J. W. Cook, R. Phillip and A. R. Somerville, *J. Chem. Soc.*, 164 (1948).

[11] E. C. S. Jones and F. L. Pyman, *ibid.*, **127**, 2588 (1925).

[12] J. v. Braun and O. Kruber, *Ber.*, **45**, 384 (1912).

[13] P. A. Plattner, *Helv. Chim. Acta*, **27**, 804 (1944).

[14] G. O. Aspinall and W. Baker, *J. Chem. Soc.*, 743 (1950).

[15] L. Schmid and F. Tadros, *Monatsh.*, **63**, 210 (1933).