free glassware; yield 0.86 g. of colorless carbinol, m. p. 126–128°. The aforementioned salt cake was treated with ice and ammonium chloride and worked up as described above. The crystallized carbinol thus obtained amounted to 3.81 g. of colorless microscopic crystals, m. p. 129–131°. The total yield was 4.67 g. or 86%. A sample purified for analysis by two recrystallizations from the same medium was obtained as colorless plates, m. p. 132–133°.

Anal. Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 84.97; H, 8.25.

1,4-Dimethylphenanthrene (VIII).—A mixture of 4.50 g. of the carbinol VI and 0.45 g. of 30% palladium–charcoal catalyst[17] was heated at 310–320° for one hour by which time 96% of the calculated volume of hydrogen was evolved. The residue was dissolved in ether, filtered and evaporated. After trituration with a few cc. of cold methanol the residue was obtained as colorless needles, m. p. 49–50.5°; yield 3.14 g. From the triturate was obtained an additional 0.59 g. of the hydrocarbon, m. p. 47.5–49.5°, making the total yield 91%. After recrystallization from methanol a sample melted at 50–51° (reported,[11] 49.5–50°). A picrate was prepared according to the reported procedure,[11] and the product had the m. p. 142.5–143.5° (reported,[11] 143.5°).

1-Methylphenanthrene (VII).—According to the procedure of Fieser and Joshel[12] for the dehydrogenation of 1-keto-2-methyl-1,2,3,4-tetrahydrotriphenylene, a mixture of 1.04 g. of 4-keto-1-methyl-1,2,3,4-tetrahydrophenanthrene (V) and 0.1 g. of 30% palladium–charcoal[17] was sealed in a tube filled with nitrogen. After heating at 320–340° for six to seven hours, the mixture was triturated with ethanol and filtered. On concentration and dilution the filtrate yielded 0.62 g. of yellow needles, m. p. 107–115°. This product was purified by conversion to the picrate and cleavage of the latter in benzene by passage through a tower of activated alumina. In this way 0.42 g. (44% yield) of colorless plates of 1-methylphenanthrene was obtained. The m. p. 116.5–118° (reported,[18] 118°) was not depressed when the sample was mixed with an authentic specimen of the hydrocarbon prepared by Dr. F. C. Meyer from 1-keto-1,2,3,4-tetrahydrophenanthrene.

Summary

Potassium *t*-butoxide has been found to be an excellent agent for promoting the Stobbe condensation of a ketone with diethyl succinate.

Procedures are given for the introduction of a propionic acid residue at the site of the carbonyl group of an aryl ketone. The steps involve (1) a Stobbe condensation with potassium *t*-butoxide, (2) acid-catalyzed decarbethoxylation of the resulting half-ester and (3) reduction.

An application of the above process to the synthesis of 2,4-dimethylphenanthrene from 2-acetylnaphthalene is described.

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(17) Linstead and Thomas, *J. Chem. Soc.*, 1127 (1940).

(18) R. D. Haworth, *ibid.*, 1125 (1932).

Madison, Wisconsin Received May 24, 1945

[Contribution from the Laboratory of Organic Chemistry of the University of Wisconsin]

The Stobbe Condensation with Tetralone-1. A Synthesis of 3′-Keto-3,4-dihydro-1,2-cyclopentenonaphthalene[1]

By William S. Johnson, Howard C. E. Johnson[2] and Jack W. Petersen

In this communication is described the first phase of a study of the use of the Stobbe condensation[3] to build up the cyclopentanone fused ring structure which is characteristic of ring D of many of the sex hormones. By this method we have succeeded in synthesizing 3′-keto-3,4-dihydro-1,2-cyclopentenonaphthalene, VI, from tetralone-1, I, in 52–54% over-all yield (Scheme A) by a process which can be carried out in a few hours. The method promises to be applicable to the synthesis of molecules more closely resembling the steroids.[4]

The various reactions which were studied are outlined in the accompanying flow sheet. The condensation of tetralone-1 (I) with diethyl succinate proceeded well in the presence of sodium ethoxide, but the reaction was much improved by the use of potassium *t*-butoxide as the condensing agent.[5] The crystalline half-ester II thus was obtained in 89–94% yields. Treatment of II with a mixture of acetic anhydride and acetic acid containing a catalytic amount of zinc chloride[6] resulted in ring closure (Scheme A) not into the aromatic nucleus, but into the unsaturated alicyclic ring to produce a keto ester, probably III (position of double bond uncertain). Like a β-keto ester (of which formula III is a vinylog) the cyclized product was decarbethoxylated readily by the action of a mixture of hydrochloric and acetic acids to give the crystalline 3′-keto-3,4-dihydro-1,2-cyclopentenonaphthalene, VI. For the over-all synthesis it was unnecessary to isolate the keto ester III; the decarbethoxylation step (III → VI) could be effected simply by the addition of dilute hydrochloric acid to the cyclization mixture followed by a short period of heating. In this way the ketone VI was obtained as the semicarbazone in 58% yield from the half-ester II.

Evidence for the structure of the ketone VI was afforded by oxidation with permanganate to phthalic acid. Had the ring closed into the benzene nucleus, the expected oxidation product would have been benzene-1,2,3-tricarboxylic acid. The nuclear structure of VI was proved conclusively by sulfur dehydrogenation to the known

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(1) This work was assisted, in part, by a grant from the Wisconsin Alumni Research Foundation.

(2) Present address: Chemical Industries, 522 Fifth Avenue, New York, N. Y.

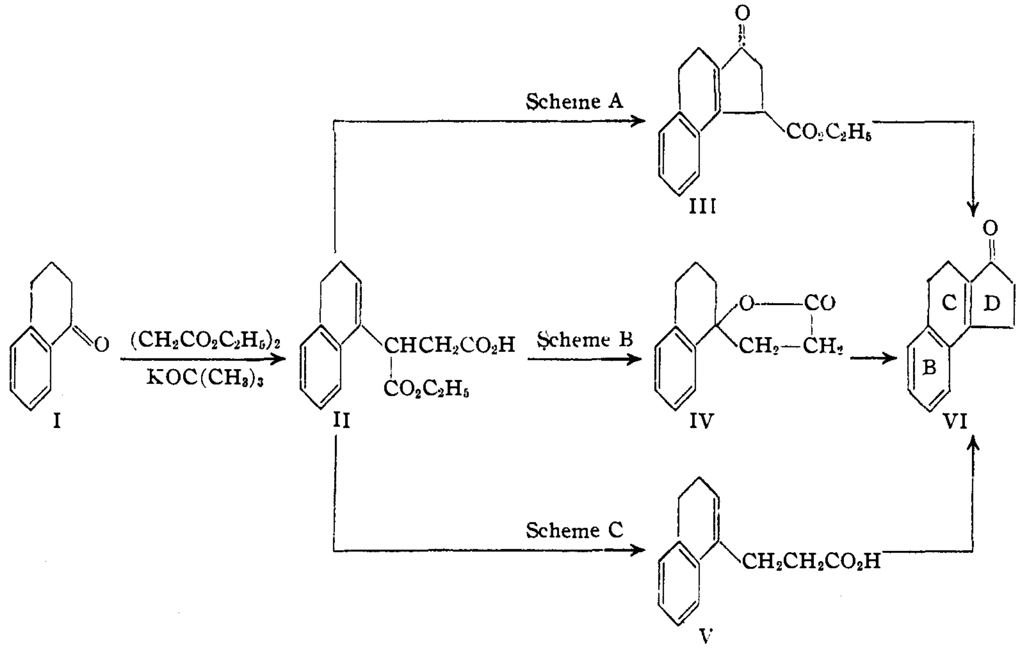
(3) *Cf.* Johnson, Goldman and Schneider, This Journal, **67**, 1357 (1945).

(4) Johnson and Petersen, *ibid.*, **67**, 1366 (1945).

(5) See ref. 3, footnote 8.

(6) *Cf.* Fieser and Hershberg, This Journal, **59**, 1028 (1937).

FLOW SHEET

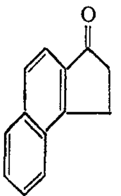


4,5-benzhydrindone-1,[7] VII, and comparisons of the ketone and oxime were made with authentic specimens kindly supplied by Dr. Fieser. The dehydrogenation of VI incidentally constitutes a good method of preparing VII. The position of the double bond in ketone VI has not been proved, but is placed between the alicyclic rings by analogy to the structure of the corresponding compound in the phenanthrene series.[4]

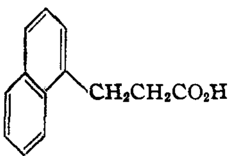
Alternate routes to the cyclic ketone involved decarbethoxylation of the half-ester II before cyclization. The cleavage was accomplished easily by the action of a mixture of hydrochloric and acetic acids. The evolution of carbon dioxide was complete after a short period of heating, and the product consisted of a simple mixture of the lactone (IV) of β-(1-hydroxy-1,2,3,4-tetrahydro-1-naphthyl)-propionic acid and the unsaturated acid V (position of double bond uncertain) which was easily separated by extraction of the latter with alkali. The proportion of lactone to acid was found to vary considerably with the reaction conditions. The results of a study of this phenomenon will appear in a future communication. In the present report a procedure is given for obtaining simultaneously the lactone IV in 38% and the acid V in 53% yield.

The position of the double bond in the unsaturated acid V is uncertain, but the remaining structure was confirmed by dehydrogenation (as the ester) to the known β-1-naphthylpropionic acid, VIII.[7] Catalytic hydrogenation of V, moreover, afforded the known β-(1,2,3,4-tetrahydro-1-naphthyl)-propionic acid, IX.[8]

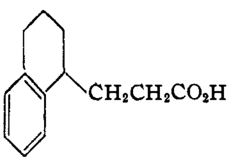
Cyclization (Scheme C) of the unsaturated acid V proceeded readily by the zinc chloride–acetic anhydride method to give the ketone VI in 76% yield. Under the same conditions the lactone IV also was cyclized (Scheme B) to give VI, but in somewhat lower (62%) yield.



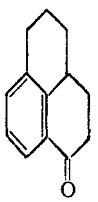
VII



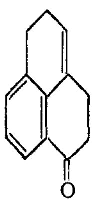
VIII



IX



X



XI

In a search for other methods of cyclization, the action of hydrogen fluoride on the acid V was investigated. Under very mild conditions (one minute in the cold) V was converted practically quantitatively into the lactone IV. When the reaction mixture was allowed to stand several

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[7] Fieser and Gates, THIS JOURNAL, 62, 2335 (1940).

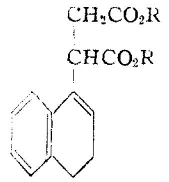
[8] v. Braun and Reutter, *Ber.*, 59, 1922 (1926).

hours at room temperature, however, cyclization was realized. In sharp contrast to the behavior with zinc chloride, very little of the ketone VI was formed. The ring closed instead mainly into the benzene nucleus giving a mixture of ketonic products from which was isolated by chromatographic adsorption 1,2,3,10-tetrahydroperinaphthanone-7 (X),[9] and a ketone of expected composition, $C_{13}H_{12}O$, which absorbed the calculated (for one double bond) amount of hydrogen in the presence of palladium-charcoal catalyst to give X. The unsaturated ketone, therefore, is assigned the structure XI. Although the position of the double bond is uncertain it is most probably not in the ketonic ring, since such a structure would be expected to isomerize to a phenol. The ketone X has been prepared previously by the aluminum chloride cyclization of the chloride of β-(1,2,3,4-tetrahydro-1-naphthyl)-propionic acid, IX (reported yield 35–45%).[8] The properties of the substance obtained in the present work were in agreement with those reported. For direct comparison we prepared the ketone X by cyclization of IX with hydrogen fluoride. The yield was 99%.

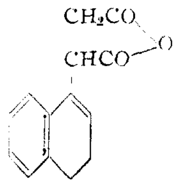
The formation of X on cyclization of V with hydrogen fluoride evidently involved disproportionation. The more highly unsaturated (dehydrogenated) material which must have been formed concomitantly with X (or with the uncyclized precursor of X) has not been isolated, but may have been represented, at least in part, by the more strongly adsorbed yellow fraction of the chromatogram which, however, was not obtained crystalline. It is not possible to decide whether the disproportionation occurred before or after cyclization. The acid V is known to be thermally susceptible to disproportionation[10] but, on the other hand, certain perinaphthanone derivatives are known to have exceptionally labile hydrogens.[7]

Haberland and Heinrich[11] have described the synthesis of a ketone which may be the 6-methoxy derivative of VI. By a Reformatsky type of reaction between β-bromopropionic ester and 6-methoxytetralone-1 they obtained β-(3,4-dihydro-6-methoxy-1-naphthyl)-propionic acid in 23–30% yield. Cyclization of this acid with phosphorus pentoxide gave the ketone which was isolated as the semicarbazone in 30% yield (over-all yield from the tetralone, 7–9%). The structure of their ketone, however, is not certain, since it has been shown in the present work that the acid V can be cyclized in both directions.

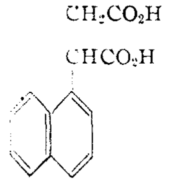
The double bond of the half-ester is pictured in the endocyclic position (pyrotartaric acid structure formula II) rather than outside the ring



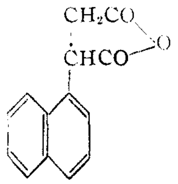
XIIa (R = H)
XIIb (R = C_2H_5)



XIII



XIV



XV

(itaconic acid structure), because of the following considerations. No tetralone-1 could be detected on mild oxidation of either the half-ester II or the dibasic acid XIIa. From a study of a large number of condensations Stobbe evolved the generalization that ketones with a methylene group flanking the carbonyl group give rise mainly to pyrotartaric acids.[12] Thus the product of the Stobbe condensation with propiophenone—which may be considered an open model of tetralone-1—was nine-tenths pyrotartaric acid derivative. Like other pyrotartaric acid derivatives[13] the dibasic acid XIIa was dehydrated to the anhydride XIII only upon heating with acetyl chloride. Itaconic acids, in contrast, generally form the anhydrides at room temperature with this reagent.[13,14]

Dehydrogenation of the full ester XIIb followed by saponification afforded 1-naphthylsuccinic acid, XIV in 89% yield. The over-all process constitutes a good synthesis of XIV. This substance has been described previously by Wislicenus[15] who reported that on fusion it lost carbon dioxide. In the present work it was found that water, not carbon dioxide, was eliminated upon fusion to form 1-naphthylsuccinic anhydride, XV.

Experimental[16]

β-Carbethoxy-β-(3,4-dihydro-1-naphthyl)-propionic Acid (II). (*a*) *By the Sodium Ethoxide Method.*—To a chilled ether suspension of 0.80 mole of alcohol-free sodium ethoxide (prepared from 18.4 g. of sodium shot and 36.8 g. of absolute alcohol in 300 cc. of dry ether) was added with vigorous stirring a solution of 58.4 g. (0.40 mole) of tetralone-1[17] and 69.6 g. (0.40 mole) of diethyl succinate in 100 cc. of dry ether. The mixture was stirred at room temperature for fifty-two hours during which it became very dark, and a heavy, red precipitate formed. Water (200 cc.) was then added, and the precipitate dissolved. Acidification of the aqueous layer liberated the dark oily half-ester. It was isolated by ether extraction, and after drying in a vacuum desiccator it was obtained as a red, gummy semi-solid. The yield of this crude material (probably still retaining some solvent) was 90.5 g. or 83%. From 4.0 g. there was obtained by

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[9] For the nomenclature see Fieser and Hershberg, THIS JOURNAL, **60**, 1658 (1938).

[10] Distillation of V at reduced pressure effects disproportionation as evidenced by the isolation of a significant amount of β-1-naphthylpropionic acid after zinc chloride catalyzed cyclization of material which had been thus treated.

[11] Haberland and Heinrich, *Ber.*, **72B**, 1222 (1939).

[12] Stobbe *Ann.*, **321**, 83 (1902).

[13] Stobbe, *ibid.*, **308**, 67 (1899).

[14] Johnson and Goldman, THIS JOURNAL, **66**, 1030 (1944).

[15] Wislicenus, Butterfass and Koken, *Ann.*, **436**, 69 (1924).

[16] All melting points are corrected.

[17] Thompson, "Organic Syntheses," **20**, 94 (1940).

three recrystallizations from dilute alcohol 2.3 g. of pure half-ester II in the form of colorless elongated prisms, m. p. 89.6–90.4°.

Anal. Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.03; H, 6.60.

When the Stobbe condensation was carried out with sodium ethoxide in refluxing alcohol, the yield of half-ester varied from 57–79%. The better yields were obtained after six hours of heating.

(*b*) *By the Use of Potassium t-Butoxide.*[3]—In a typical run 7.3 g. (0.050 mole) of tetralone-1 ($n^{15}D$ 1.5704) and 13.05 g. (0.075 mole) of diethyl succinate were added with 10 cc. of *t*-butyl alcohol (to aid in transfer) to a chilled solution of 2.15 g. (0.055 mole) of potassium in 40 cc. of dry *t*-butyl alcohol. The brownish red solution was then allowed to reflux (oil-bath at 110°) for forty minutes in a system which had been previously evacuated, filled with nitrogen and sealed from the atmosphere by a mercury trap. After cooling the mixture was acidified with dilute hydrochloric acid, and the solvent was removed at slightly reduced pressure. The semi-solid, straw-colored residue was taken up in ether, washed with water and the washings were re-extracted with ether. The combined ether solutions were extracted thoroughly with saturated sodium bicarbonate solution. These aqueous solutions were combined, washed once with ether, and then acidified. The pink oil which separated soon set to a straw-colored solid which was filtered. After trituration with 20 cc. of water the dried material amounted to 12.25 g. (89% yield), m. p. 64–69°. In other runs yields as high as 94% were realized. Recrystallization of 0.500 g. of this material from dilute methanol afforded 0.445 g. of colorless needles m. p. 73–75°. This evidently corresponded to an unstable polymorphic form of the material described above under *a*, for after standing for some time it had changed over to the higher-melting form, m. p. 89.5–91°, undepressed by the material described under *a* above. When the oil which separated upon acidification of the bicarbonate solutions was seeded with the higher-melting modification, the crude half-ester melted at 82–86°.

When the condensation was carried out with equimolar quantities of ketone and ester the best yields of half-ester which were obtained after one hour refluxing (optimum time) were 54–58%. Increasing the molar proportion of potassium *t*-butoxide did not improve the yield and afforded a slightly less pure product.

Decarbethoxylation of β-Carbethoxy-β-(3,4-dihydro-1-naphthyl)-propionic Acid.—A solution of 1.0 g. of the crude (from procedure *b*) half-ester II in 7 cc. of acetic acid, 3.5 cc. of concentrated hydrochloric acid and 5 cc. of water was boiled under reflux for four and one-half hours. Copious evolution of carbon dioxide was noted during the first hour of heating. The mixture was concentrated under reduced pressure and the semi-solid, straw-colored residue was worked up by ether extraction followed by thorough extraction with bicarbonate solution. Acidification of the bicarbonate solutions afforded 0.39 g. (53% yield) of colorless **β-(3,4-dihydro-1-naphthyl)-propionic acid (V)**, m. p. 102–105°. One gram of this material recrystallized from dilute methanol gave a total of 0.90 g. of colorless thin tablets m. p. 105.5–107°. The best sample obtained after several recrystallizations melted at 106.8–107.5°.

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98; neut. equiv., 202.2. Found: C, 77.29; H, 6.76; neut. equiv., 200.5, 202.2.

The combined ether (neutral) solutions were dried over anhydrous sodium sulfate and evaporated. Thus was obtained 0.28 g. (38% yield) of crude, straw-colored lactone IV, m. p. 50–55°. Recrystallization from ether-petroleum ether (b. p. 40–60°), afforded 0.175 g. of colorless flat rods, m. p. 64–66°. The analytical sample of the **lactone (IV) of β-(1-hydroxy-1,2,3,4-tetrahydro-1-naphthyl)-propionic acid** melted at 64.5–65.5°.

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.03; H, 7.09.

The lactone IV dissolves in warm aqueous alkali. Acidification of such a solution with mineral acid gives a mixture of lactone IV and unsaturated acid V. All attempts to prepare the hydroxy acid failed.

3′-Keto-3,4-dihydro-1,2-cyclopentenonaphthalene (VI). (*Scheme A*) *Cyclization of β-Carbethoxy-β-(3,4-dihydro-1-naphthyl)-propionic Acid.*—A solution of 1.000 g. of the crude (from procedure *b*) half-ester (II), in 10 cc. of acetic anhydride and 5 cc. of a stock solution of fused zinc chloride (20 mg. per cc.) in glacial acetic acid was allowed to reflux in an atmosphere of nitrogen for three and one-half hours. The excess acetic anhydride was then decomposed by the cautious addition of 10 cc. of water to the red solution. To cleave the keto ester 4 cc. of concentrated hydrochloric acid was added to the cooled solution and the mixture was allowed to reflux for forty-five minutes during which carbon dioxide was evolved rapidly. The solvent was removed under reduced pressure, and the dark residue was warmed for thirty minutes on the steam-bath with 20 cc. of 5% potassium hydroxide solution in order to cleave any lactone. The remaining neutral oil was extracted with ether, washed with dilute alkali, and dried over anhydrous sodium sulfate. The brownish oily residue obtained upon evaporation of the ether soon crystallized. Purification of small amounts of the crude ketone was effected readily by conversion to the sparingly soluble semicarbazone. Thus the material above was heated in 10 cc. of ethanol containing 1 g. of semicarbazide hydrochloride and 1 cc. of pyridine at 75° for thirty minutes. Almost colorless semicarbazone of VI was obtained on dilution; yield 0.510 g. (58%); m. p. 273.5–274.2° (dec.) (introduced in bath at 265°). Recrystallization from glacial acetic acid afforded colorless prisms which were photosensitive, turning bright yellow on exposure to light.

Anal. Calcd. for $C_{14}H_{15}ON_3$: C, 69.69; H, 6.27. Found: C, 69.57; H, 6.14.

Cleavage of the semicarbazone with 20% hydrochloric acid afforded the ketone, m. p. 78–80°, in practically quantitative yield. Recrystallization from dilute alcohol gave colorless prisms, m. p. 80.8–81.2°.

Anal. Calcd. for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.91; H, 6.55.

When the nitrogen was omitted in the cyclization step, the yield of semicarbazone dropped to 0.395 g. (45%) of darker material m. p. 270.8–271.2° (dec.).

In another experiment the procedure described above was followed up through the hydrolysis of the acetic anhydride. Instead of being decarbethoxylated, the product was worked up by removing the solvent under reduced pressure. The dark oily residue was taken up in ether, and washed with saturated sodium bicarbonate solution which removed a trace of acidic material. The ether solution was washed with water, dried over anhydrous sodium sulfate, and evaporated. The light-brown oil was converted to the **semicarbazone** of **ethyl 3′-keto-3,4-dihydro-1,2-cyclopentenonaphthalene-1′-carboxylate (III)** by the procedure described above for VI. The slightly yellow crystalline derivative amounted to 0.710 g. (62%) and melted at 227.2–231.5° (dec.) (introduced in bath at 220°). Recrystallization from chloroform gave colorless prisms which turned bright yellow on exposure to light.

Anal. Calcd. for $C_{17}H_{19}O_3N_3$: C, 65.16; H, 6.11. Found: C, 65.11; H, 6.09.

When nitrogen was not used in the cyclization step the yield was 0.470 g. (41%) of material melting at 227–230° (dec.) (introduced in bath at 220°).

(*Scheme B*) *Cyclization of the Lactone (IV) of β-(1-Hydroxy-1,2,3,4-tetrahydro-1-naphthyl)-propionic Acid.*—A solution of 1.000 g. of the lactone (IV), m. p. 64–66°, in 16 cc. of acetic anhydride, 5 cc. of stock solution of fused zinc chloride (20 mg. per cc.) in acetic acid and 5 cc. of acetic acid, was allowed to reflux in an atmosphere of nitrogen for four and one-half hours. After cooling the mixture was treated with water, and the solvent removed under reduced pressure. The brown residue was warmed for one hour on the steam-bath with 20 cc. of 5% potassium hydroxide, extracted with ether and treated with Norit. The residue obtained upon evaporation was converted to the semicarbazone as described above. The yellow crystalline product amounted to 0.735 g. (62% yield), m. p. 271.5–273° (dec.) (introduced at 265°). When the reaction was carried out in the absence of nitrogen the yield was 36%.

(Scheme C) Cyclization of β-(3,4-Dihydro-1-naphthyl)-propionic Acid (*V*).—One gram of the acid V, m. p. 104–107°, was treated by the procedure described above for cyclization of the lactone (Scheme B). The yield of semicarbazone was 0.905 g. (76%) of tan crystals, m. p. 272.2–273° (dec.) (introduced at 265°). When the cyclization was conducted without nitrogen the yield dropped to 61%.

Dehydrogenation of Ketone VI to 4,5-Benzhydrindone-1 (VII).—A mixture of 0.688 g. of the ketone VI, m. p. 73–77°, and 0.120 g. of sulfur was heated at 220°. After one hour the evolution of hydrogen sulfide had practically ceased, and the product was sublimed at reduced pressure. The yellow solid sublimate amounted to 0.460 g., m. p. 107–111°. It was converted to the colorless crystalline semicarbazone (0.460 g. or 51.5% yield), m. p. 267–268°, which was hydrolyzed by warming on the steam-bath for twenty minutes with 20% hydrochloric acid. As the derivative was cleaved the benzhydrindone VII crystallized in the form of colorless elongated prisms, m. p. 113–116°. Twice recrystallized from benzene–petroleum ether the product was obtained as colorless needles, m. p. 119.6–120.3° (reported,[7] 120.6–121.4° (cor.)). The sample of 4,5-benzhydrindone-1 supplied to us by Dr. Fieser melted at 118.6–120.6°, and a mixture with our ketone melted at 119.6–120.6°. The oxime of VII was also prepared for comparison. It crystallized from ethyl acetate in the form of heavy colorless prisms, m. p. 228.5–230° (reported[7] 229–231° (cor.)). This same m. p. was also found for the sample of Fieser and Gates as well as for the mixture of the two.

Oxidation of Ketone VI to Phthalic Acid.—A mixture of 0.79 g. of the ketone VI and 7.4 g. of potassium permanganate in 65 cc. of water was allowed to reflux for forty-five minutes. The cooled solution was acidified with sulfuric acid and the suspended manganese dioxide was decomposed with sodium bisulfite. Ether extraction afforded 0.58 g. of a gummy solid, a portion of which on sublimation and recrystallization from petroleum ether gave colorless crystals, m. p. 128–130°. A mixture with phthalic anhydride (m. p. 130–131°) melted at 128–130°.

Dehydrogenation of V to β-1-Naphthylpropionic Acid.—Esterification of 5.5 g. of β-(3,4-dihydro-1-naphthyl)-propionic acid (V) was carried out in 30 cc. of alcohol and 50 cc. of benzene containing 4 drops of concentrated sulfuric acid. A previously described technique involving the use of a continuous water separator was used.[14] The product amounted to 4.7 g. (75% yield) of oil, b. p. 145–150° (2–3 mm.). Two grams of this material was heated at 300° with 0.2 g. of 30% palladium–charcoal catalyst[18] until hydrogen was no longer evolved. Saponification of the resulting oil with 10% methanolic potassium hydroxide solution afforded 1.52 g. (an 87% yield) of colorless crystalline acid, m. p. 153–154°. After recrystallization from dilute alcohol the substance melted at 154–154.5° (reported m. p. 156–156.7° (cor.))[7]. The amide was prepared by ammonolysis of the acid chloride. The m. p. was 103–104° (reported,[7] 103–104° (cor.)).

Diethyl (3,4-Dihydro-1-naphthyl)-succinate (XIIb).—Esterification of 20.0 g. of the crude half-ester II prepared by procedure *a* above was effected with 40 cc. of alcohol and 80 cc. of benzene containing 5 drops of concentrated sulfuric acid. The technique involving the use of a continuous water separator was used.[14] The yield of pale yellow diethyl ester was 18.4 g. (84% yield), b. p. 189–193° (2–3 mm.).

Anal. Calcd. for $C_{18}H_{22}O_4$: C, 71.50; H, 7.34. Found: C, 71.40; H, 7.26.

After standing for two days the above product solidified, m. p. 34–36°. Recrystallization from dilute alcohol afforded colorless plates, m. p. 35.3–36.4°.

(3,4-Dihydro-1-naphthyl)-succinic Acid (XIIa).—Four grams of crude half-ester II (prepared by procedure *a*) was saponified in 20 cc. of 10% sodium hydroxide solution. After refluxing for six hours in an atmosphere of nitrogen, the mixture was acidified. Recrystallization of the crude dibasic acid from dilute alcohol gave 2.8 g. (a 78% yield) of material melting at 174–178° (dec.). On further recrystallization the acid was obtained as colorless prisms, m. p. 182–182.7° (dec.).

Anal. Calcd. for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.43; H, 5.64.

(3,4-Dihydro-1-naphthyl)-succinic Anhydride (XIII).—A solution of 0.214 g. of the above acid XIIa, m. p. 179–181° (dec.), in 3 cc. of acetyl chloride was allowed to reflux for one hour. Evaporation of the solvent left an oily residue (0.194 g.) which solidified on scratching, m. p. 88–94°. Recrystallization from benzene–petroleum ether afforded colorless prisms, m. p. 93.5–95°; yield 0.127 g. Twice recrystallized from carbon bisulfide the material melted at 95.4–96.6°.

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.60; H, 5.21.

When a solution of the dibasic acid in acetyl chloride was allowed to stand at room temperature for twenty hours no anhydride formation was observed. The residue after evaporation melted at 177–179° (dec.).

1-Naphthylsuccinic Acid (XIV).—A mixture of 10.0 g. of diethyl 3,4-dihydro-1-naphthylsuccinate and 1 g. of 30% palladium–charcoal catalyst[18] was heated at 260–270° in a system which was previously evacuated and filled with nitrogen. After two hours hydrogen ceased to be evolved, and the cooled product was taken up in ether and filtered. The oil obtained on evaporation was saponified with methanolic potassium hydroxide. The acidic material obtained after ten hours of refluxing amounted to 7.2 g. (89% yield), m. p. about 200–205° (dec.). A sample was purified by repeated recrystallization from water. The glistening colorless blades melted with decomposition over a range which depended on the rate of heating. For example, when introduced into the bath at 200° the m. p. was about 215–220° (reported 205–206°[15]). The homogeneity of this substance was established, however, by conversion to the sharp-melting anhydride described below.

Anal. Calcd. for $C_{14}H_{12}O_4$: C, 68.85; H, 4.95. Found: C, 69.10; H, 4.99.

In order to ascertain the nature of the decomposition which attended fusion of the acid, a sample (about 0.5 g.) was melted in a test-tube with a side-arm leading into barium hydroxide solution. The apparatus was swept out with nitrogen before decomposition began. No clouding of the barium hydroxide solution was observed, but moisture collected on the walls of the tube. The residue was crystallized from carbon bisulfide. The melting point of the product was 125.5–127.5° and was not depressed on mixing with 1-naphthylsuccinic anhydride described below.

Dehydrogenation of the ester XIIb (25 g.) was also carried out at 275° for ten hours in a bomb with benzene and nickel-Kieselguhr catalyst.[19] The yield of naphthylsuccinic acid by this method was 65% (13.2 g.).

1-Naphthylsuccinic Anhydride (XV).—The dehydration of 0.184 g. of 1-naphthylsuccinic acid was effected with 3 cc. of acetyl chloride as described above for the dihydro derivative. The crude product (0.159 g.) melted at 112–118°. Recrystallization from benzene-petroleum ether gave 0.134 g. (79% yield) of colorless crystals, m. p. 127–128.5°. After two recrystallizations from carbon bisulfide the product was obtained as rectangular plates, m. p. 128.6–129.4°.

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.33; H, 4.46. Found: C, 74.27; H, 4.45.

Oxidation of the half-ester II was carried out at 0° with two molar equivalents of 2% potassium permanganate solution according to the procedure of Stobbe.[20] The

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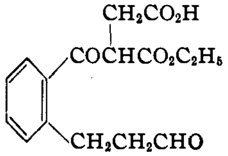
[18] Linstead and Thomas, *J. Chem. Soc.*, 1127 (1940).

[19] Adkins, Richards and Davis, This Journal, **63**, 1320 (1941).

[20] Stobbe, *Ann.*, **308**, 123 (1899).

product was mainly acidic, and no tetralone semicarbazone was obtained when the neutral fraction was treated with semicarbazide. Similar results were obtained when the dibasic acid XIIa was oxidized.

In another experiment 0.5 g. of the half-ester II dissolved in 20 cc. of ethyl acetate was treated with ozone at 0° until a test with starch–iodide paper indicated an excess of oxidizing agent. The solvent was evaporated and replaced by ether, and the ozonide was decomposed by stirring with Raney nickel.[21] The filtered solution was extracted with saturated sodium bicarbonate solution. Evaporation of the ether left only a trace of oil which failed to form a semicarbazone. Acidification of the bicarbonate extracts afforded an oil which could not be crystallized. It gave a cherry red color with ferric chloride and may have contained some of the aldehydo acid (A), which, being also a β-keto ester, could give a ferric chloride test.



(A)

β-(1,2,3,4-Tetrahydro-1-naphthyl)-propionic Acid (IX).—von Braun and Reutter[8] have prepared this acid by a six-step synthesis from tetralone-1 *via* the Reformatsky reaction. In the present work β-(3,4-dihydro-1-naphthyl)-propionic acid (0.212 g.) was hydrogenated in the presence of palladium–charcoal catalyst.[18] The yield of reduced acid after recrystallization from petroleum ether was 84% (0.180 g.), m. p. 79–82° (reported,[8] 83°). This material was satisfactory for the cyclization step described below.

Cyclization of IX to 1,2,3,10-Tetrahydroperinaphthanone-7 (X).—One-tenth of a gram of β-(1,2,3,4-tetrahydro-1-naphthyl)-propionic acid, m. p. 79–82°, was treated with an excess of anhydrous hydrogen fluoride according to a procedure previously described.[22] The neutral product amounted to 0.09 g. (99% yield) of the ketone X, m. p. 67–70°. It formed colorless elongated prisms from dilute alcohol, m. p. 69.2–70° (reported[8] 72°). The semicarbazone was obtained as colorless tablets, m. p. 230.5–231.7° (reported[8] 235°).

The Action of Hydrogen Fluoride on β-(3,4-Dihydro-1-naphthyl)-propionic Acid. (a) **Lactonization.**—To 1.000 g. of the acid V (m. p. 105–107°) contained in a platinum vessel which was chilled in an ice–salt-bath was added 15 to 20 cc. of anhydrous hydrogen fluoride. After swirling for one minute the solution was evaporated in a current of air, and saturated sodium bicarbonate solution was added. The organic residue was taken up in ether, washed with saturated sodium bicarbonate solution and dried over anhydrous sodium sulfate. Evaporation afforded 0.945 g. (94% yield) of crystalline lactone IV, m. p. 57.5–61°. Recrystallization from ether–petroleum ether (b. p. 40–60°) gave colorless material, m. p. 65–67°, undepressed by the sample of lactone described above.

(b) **Cyclization.**—A solution of 3.65 g. of the acid V in about 50 cc. of anhydrous hydrogen fluoride was allowed to stand in a platinum vessel at room temperature for sixteen hours. The excess solvent was removed by evaporation, and the residue was taken up in ether and washed thoroughly with 10% potassium hydroxide solution. Acidification of these alkaline extracts gave only a trace of organic acid. The semi-solid neutral material, obtained upon evaporation of the ether solution, was treated with 25 cc. of methanol, 3.0 g. of semicarbazide hydrochloride and 2.3 cc. of pyridine. After refluxing for one hour the solution was cooled, and 1.29 g. of crude yellow semicarbazone, m. p. 205–220°, crystallized. This was cleaved by boiling with 20% hydrochloric acid for ten minutes, and the resulting ketone was separated by ether extraction. The dried ketone was dissolved in dry benzene and subjected to chromatographic adsorption on a column of activated alumina. No crystalline material was obtained from the highly adsorbed dark zones. Elution of the larger yellow zone with acetone–alcohol afforded 0.71 g. of crystalline ketone, m. p. 55–65°. Crystallization from benzene–petroleum ether gave 0.37 g., m. p. 66–69°, and recrystallization from dilute alcohol afforded 0.29 g. of light-yellow material, m. p. 67–70°.

Anal. Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 84.02; H, 7.36.

The above material apparently was 1,2,3,10-tetrahydroperinaphthanone-7 (X) containing a trace of yellow impurity. The mixed m. p. with the colorless sample of X (m. p. 69.2–70°), obtained by the conventional synthesis described above, was 67–70°.

Isolation of a Dihydroperinaphthanone (Possibly XI).—The mother liquor from the semicarbazone reaction was evaporated, and the solid residue washed well with water, dried and triturated with benzene. This left 1.35 g. of crude semicarbazone, m. p. 190–200°, which was cleaved with 20% hydrochloric acid at room temperature for two days. The resulting ketone was isolated and chromatographed in the manner described above. Elution of the strongly adsorbed yellow zone gave an intractable oil. The colorless, fluorescent (in ultraviolet light) zone, however, afforded 0.61 g. of gummy solid which was recrystallized from dilute methanol. Thus was obtained 0.15 g. of long, slightly yellow needles, m. p. 60–62°. Recrystallization gave almost colorless needles, m. p. 63–65°. A mixture with 1,2,3,10-tetrahydroperinaphthanone (X) melted at 56–60°.

Anal. Calcd. for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.78; H, 6.18.

Catalytic hydrogenation of 0.061 g. of the above ketone in ethyl acetate (10 cc.) in the presence of 0.06 g. of 30% palladium–charcoal catalyst[18] was complete in three and one-half hours. An amount of hydrogen calculated to saturate one double bond was absorbed. The oil obtained on evaporation of the filtered solution, was treated with 4 cc. of methanol, 0.05 g. of semicarbazide hydrochloride and 6 drops of pyridine. After refluxing for one hour the solution was evaporated, and the residue was washed with water and with ether. The colorless semicarbazone which remained amounted to 0.02 g., m. p. 230–231°. An additional 0.015 g. of material, m. p. 228–232°, was recovered from the ether washings. No depression of the m. p. was observed on admixture with the semicarbazone of X which is described above. Hydrolysis of this derivative (0.02 g.) with 0.5 cc. of 20% hydrochloric acid afforded 0.01 g. of ketone, m. p. 66–69°. A mixture with pure X melted at 67–70°.

Isolation of 3′-Keto-3,4-dihydro-1,2-cyclopentenonaphthalene (VI).—In the cyclization experiment just described it was noticed that during the semicarbazone formation of the crude product some material precipitated while the reaction mixture was refluxing. In another cyclization of 1.132 g. of the dihydronaphthylpropionic acid, this sparingly soluble fraction was filtered from the hot solution. It amounted to 0.095 g. (7% yield) and melted at 260–262° (dec.). A mixture with the semicarbazone of VI showed no depression of the m. p.

In other cyclization experiments all attempts to separate the ketones by fractional crystallization met with failure. Almost invariably an apparently homogeneous product, m. p. *ca.* 70°, was obtained. The analyses of various samples were inconsistent, and it was shown by chromatographic analysis that these were mixtures.

Summary

The Stobbe condensation between tetralone-1 and diethyl succinate has been found to proceed in excellent yield when potassium *t*-butoxide is used as the condensing agent. Zinc chloride-

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(21) Cook and Whitmore, THIS JOURNAL, **63**, 3540 (1941).

(22) Adams, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 157.

catalyzed cyclization of the resulting half-ester, followed by acid hydrolysis affords 3′-keto-3,4-dihydro-1,2-cyclopentenonaphthalene in 52–54% over-all yield from tetralone-1.

Acetic–hydrochloric acid hydrolysis of the half-ester effects the loss of the carbethoxyl group to produce β-(3,4-dihydro-1-naphthyl)-propionic acid and the corresponding lactone. These substances can be cyclized by the zinc chloride method also to give the cyclopentenonaphthalene derivative. Hydrogen fluoride, in contrast, promotes ring closure mainly into the aromatic nucleus to give perinaphthanone derivatives.

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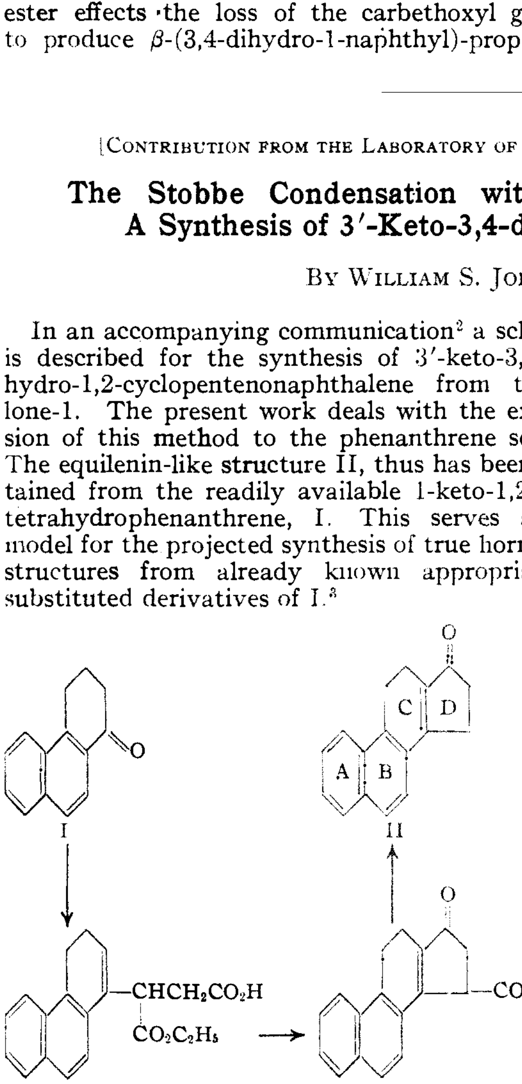
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Stobbe Condensation with 1-Keto-1,2,3,4-tetrahydrophenanthrene. A Synthesis of 3′-Keto-3,4-dihydro-1,2-cyclopentenophenanthrene[1]

BY WILLIAM S. JOHNSON AND JACK W. PETERSEN

In an accompanying communication[2] a scheme is described for the synthesis of 3′-keto-3,4-dihydro-1,2-cyclopentenonaphthalene from tetralone-1. The present work deals with the extension of this method to the phenanthrene series. The equilenin-like structure II, thus has been obtained from the readily available 1-keto-1,2,3,4-tetrahydrophenanthrene, I. This serves as a model for the projected synthesis of true hormone structures from already known appropriately substituted derivatives of I.[3]



Like tetralone-1,[2] 1-keto-1,2,3,4-tetrahydrophenanthrene condensed readily with diethyl succinate in the presence of potassium *t*-butoxide.[4] The yield of crystalline half-ester was 88%, and the structure III is suggested by analogy to the probable structure of the corresponding half-ester in the naphthalene series.[2] Cyclization with zinc chloride in acetic acid and acetic anhydride afforded a keto ester, probably IV (position of double bond uncertain), which on acid hydrolysis, readily lost the carbethoxyl group to give 3′-keto-3,4-dihydro-1,2-cyclopentenophenanthrene, II. Without isolation of the keto ester the over-all yield of II from the half-ester III was 50%. This ketone is probably identical with the one obtained by Bardhan[5a] (in unspecified yield) through the Bougault cyclization of the keto ester Va followed by pyrolytic ring closure of the resulting dicarboxylic acid; and with the product prepared by Robinson and Thompson[5b] (in 15% yield) from the keto ester Vd; and also with the ketone synthesized by Bachmann, Gregg and Pratt[5c] through Bougault cyclization (in 15–23% yield) of Vc followed by decarboxylation and Dieckmann cyclization of the dicarboxylic ester. Although the yields of II obtained by the previous methods[5] are low in comparison with those realized in the present work, it should be noted that the cyclization of keto esters like V is generally improved by the activating influence of a methoxyl group in the 6 position of the naphthalene nucleus.[5c] The melting points reported for the various specimens of II are 210,[5a] 212–213°,[5b] and 214–216°.[5c] The ketone obtained in the present work melted at 222.5–223.3° (cor.), the semicarbazone at 316–317°, and the oxime at 254.5–255°.

Nitric acid oxidation of the semicarbazone of IV gave benzene-1,2,3,4-tetracarboxylic acid, evidently arising from ring B, thus indicating that the ring closure had taken place into the alicyclic rather than into the aromatic nucleus. Conclusive proof of the nuclear structure was afforded by the degradation which Bardhan[5a] used, namely, Clemmensen reduction followed by dehydrogenation to give the known 1,2-cyclopentenophenanthrene. The ultraviolet absorption spectrum of the ketone has been obtained by Dr. A. L. Wilds and his collaborators.[6] The results of this work which will be published in the near future indicate beyond reasonable doubt that the double

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(1) This work was assisted, in part, by a grant from the Wisconsin Alumni Research Foundation.

(2) W. S. Johnson, H. C. E. Johnson and Petersen, THIS JOURNAL, **67**, 1360 (1945).

(3) The preliminary results of work in progress on some of these derivatives of I are promising.

(4) *Cf.* Johnson, Goldman and Schneider, THIS JOURNAL, **67**, 1357 (1945).

(5) (a) Bardhan, *J. Chem. Soc.*, 1848 (1936); (b) Robinson and Thompson, *ibid.*, 1739 (1939); (c) Bachmann, Gregg and Pratt, THIS JOURNAL, **65**, 2314 (1943).

(6) Wilds, Beck, Close, Djerassi, J. A. Johnson and T. L. Johnson.