A two-step mechanism has been suggested for this reaction which is to be classified as a "hydrogen transfer reaction."

As an acceptor for the hydrogen transferred, foreign substances can be used. As an example, mesityl oxide was investigated as hydrogen acceptor.

The dismutation is accompanied by direct dehydrogenation of limonene to *p*-cymene. This reaction seems to be accelerated by the presence of mesityl oxide.

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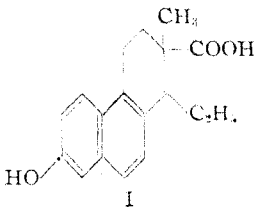
[JOINT CONTRIBUTION FROM THE JEFFERSON MEDICAL COLLEGE AND THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Improvement of the Synthesis of Bisdehydrodoisynolic Acid[1]

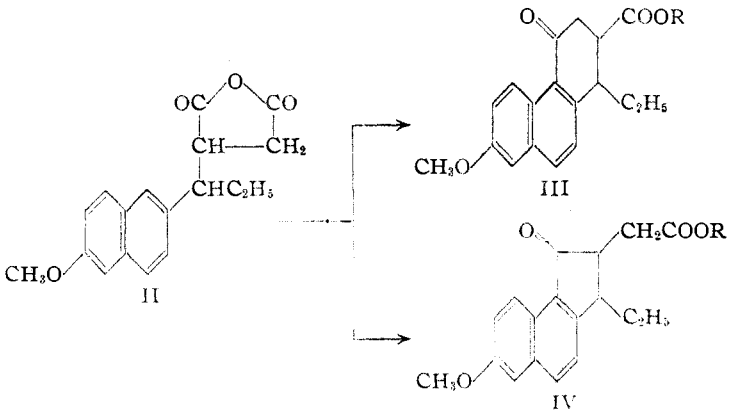
BY D. L. TURNER, BIDYUT KAMAL BHATTACHARYYA,[2] ROBERT P. GRABER[3] AND WILLIAM S. JOHNSON

In our recent synthesis of the potent estrogen bisdehydrodoisynolic acid[4] (I) all of the steps were satisfactory except for the cyclization of the an-



I

hydride II which gave the desired phenanthrene ketone III (R = H) in at best 20% yield. The main product was the isomeric benzhydrindone



II III IV

IV (R = H) arising from five- instead of six-membered ring closure. These findings have been confirmed in essence by Heer and Miescher[5] who, using our earlier method,[4a] obtained III (R = H) in only about 8% yield.

In the present communication we are describing a study which not only has led to a striking improvement in the cyclization step, but at the same time has reduced the total number of steps in the synthesis to seven starting from 2-methoxynaphthalene. These objectives were realized as the result of the discovery that the half-ester VI can be cyclized to give almost exclusively the desired keto ester III (R = CH_3). The total 7-step synthesis is depicted in the accompanying flow sheet.

The crystalline half-ester VI was prepared easily in 52% over-all yield by hydrogenation of the crude oily mixture of half-esters produced by the Stobbe condensation of 2-propionyl-6-methoxynaphthalene (V) with dimethyl succinate. This half-ester was identical with material produced by selective saponification of the dimethyl ester resulting from the action of diazomethane on the 165° dibasic acid (corresponding to formula VI) previously described.[4] When a benzene solution of VI was treated for 45 minutes in the cold with phosphorus pentachloride, then for 10 minutes at 0° with stannic chloride,[6] cyclization occurred giving the crystalline keto ester III (R = CH_3) of good purity in 67% yield. The identity was confirmed by mixed melting point comparison of the ester and the free acid (obtained on saponification) with authentic specimens described previously.[4] Since the keto ester III (R = CH_3) is known to be easily convertible by hydrogenolysis into the ester VII which upon methylation and hydrolysis yields bisdehydrodoisynolic acid I,[4] the synthesis is thus completed.

(1) This work was assisted in part by grants from the American Cancer Society, recommended by the Committee on Growth of the National Research Council, and from the Research Committee of the Graduate School of the University of Wisconsin from funds supplied by the Wisconsin Alumni Research Foundation.

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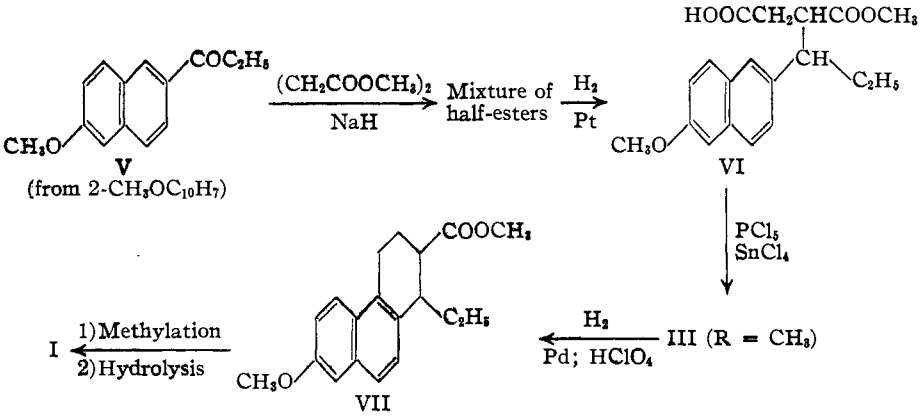
(4) Johnson and Graber, THIS JOURNAL, (a) **70**, 2612 (1948); (b) **72**, 925 (1950).

(5) Heer and Miescher, *Helv. Chim. Acta*, **33**, 178 (1950); "Auf jeden Fall ist die Tatsache festzuhalten, dass die elegante und relativ kurze Synthese von Johnson and Graber nur in untergeordneter Ausbeute wirksame α-Bisdehydro-doisynolsäure ergibt, zur Hauptsache aber zu unwirksamer Cyclopentano-naphtalin-essigsäure führt."

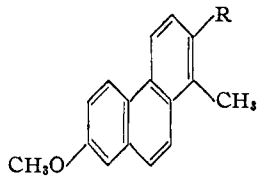
(6) *Cf.* Fieser and Novello, THIS JOURNAL, **62**, 1855 (1940).



The yield of III (R = CH_3) actually formed in the cyclization described above is higher than 67% since an additional 6% of crude material was obtained as a second crop in the crystallization. The third crop contained the isomeric keto ester IV (R = CH_3) which was isolated in about 1% yield and identified by comparison (mixed melting point) with an authentic specimen.[4] The formation of IV (R = CH_3) from VI undoubtedly involves a rearrangement (possibly during preparation) of the intermediary half-ester chloride.[7] Since this type of rearrangement has been shown to be facilitated by heat,[7] it was not surprising to find that the ratio of IV (R = CH_3) to III (R = CH_3) was raised significantly when the cyclization of VI was conducted as described above except that the phosphorus pentachloride treatment was carried out with heating. Similar results were obtained when thionyl chloride was used to prepare the acid chloride, the product IV (R = CH_3) being isolated only when the reaction temperature was higher.

A similar cyclization study was also made with the lower homolog VI (CH_3 in place of C_2H_5). The Stobbe condensation with 2-acetyl-6-methoxynaphthalene (V, CH_3 in place of C_2H_5) and dimethyl succinate afforded a mixture of half-esters[8] from which one isomer, m. p. 160–162° after purification, was crystallized in 23% yield. Hydrogenation of this product gave the α-half-ester VI (CH_3 in place of C_2H_5), m. p. 121–122° (α-dibasic acid, m. p. 158–160°; α-dimethyl ester, m. p. 57–59°). A diastereoisomeric β-form of the half-ester VI (CH_3 in place of C_2H_5) was prepared as follows. The oily half-ester remaining after removal of the crystalline fraction from the Stobbe condensation product described above was hydrogenated, and a portion (23% yield based on starting ketone) of the resulting mixture was obtained crystalline. This material, however, could not be successfully purified by recrystallization so was saponified giving the β-dibasic acid, m. p. 188–190° after recrystallization, diastereoisomeric with the α-dibasic acid. Esterification of the β-dibasic acid yielded the β-dimethyl ester, m. p. 88–90°, which on selective saponification yielded the β-half-ester VI (CH_3 in place of C_2H_5), m. p. 160–162°.

Cyclization of the α- and β-half-esters by essentially the same procedure as used for the higher homolog, gave, respectively, the α- (m. p. 110–111°) and β- (m. p. 114–115.5°) forms of keto ester III (R = CH_3, in place of C_2H_5). This structure was suggested for these products by the similarity of their ultraviolet absorption spectra with that of the compound III (R = H) in the bisdehydrodoisynolic acid series, and was proved by conversion of both these substances *via* the 4-desoxy compounds (see below) to 1-methyl-7-methoxyphenanthrene VIII (R = H), which was compared



VIII

with authentic material[9] kindly supplied by Professor W. E. Bachmann. The α- and β-stereoisomeric keto esters showed a surprising difference in reactivity of the carbonyl group toward semicarbazide; the former failed to form any of the derivative under normally severe conditions. This behavior may possibly mean that in the α-isomer the $COOCH_3$ prefers to lie in the erected (polar) position which is likely only if the $COOCH_3$ and 1-CH_3 groups are *cis*.

Acid-promoted catalytic hydrogenolysis of the α- and β-isomers of the keto ester yielded the corresponding α- (m. p. 115–116.5°) and β- (m. p. 109–111°) forms of the ester VII (CH_3 in place of C_2H_5). One of these is probably identical with the product m. p. 110–112°, prepared by Anner and Miescher[10] by a different synthesis.

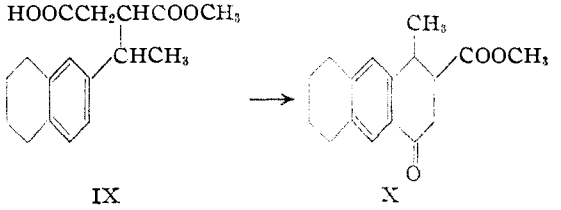
The α- and β-forms of VII (CH_3 in place of C_2H_5) were shown to be different by a marked depression of the m. p. on admixture. Dehydrogenation of the latter with palladium catalyst at 250° afforded a product agreeing in properties with Anner and Miescher's[10] methyl 1-methyl 7-methoxyphenanthrene-2-carboxylate VIII (R = $COOCH_3$).

(7) *Cf.* Cason, *ibid.*, **69**, 1548 (1947); Ställberg-Stenhagen, *ibid.*, **69**, 2568 (1947).

(8) The mixture probably consists largely of *cis* and *trans* isomers as proved in the case of 2-acetylnaphthalene, Johnson and Goldman, THIS JOURNAL, **66**, 1030 (1944).

(9) Bachmann and Chemerda, *ibid.*, **70**, 1468 (1948).

(10) Anner and Miescher, *Helv. Chim. Acta*, **29**, 586 (1946).



IX X

The technique described in this paper has been extended further to include the cyclization of the crystalline half-ester IX, m. p. 142-144°, which was prepared by selective saponification of the corresponding dimethyl ester recently described.[11] Ring closure of IX as described above yielded the keto ester X identical with material prepared previously *via* cyclization of the anhydride.

Acknowledgment.—We are indebted to Mrs. R. P. Gerhart for technical assistance.

Experimental Part[12,13,14]

3-Carbomethoxy-4-(6-methoxy-2-naphthyl)-caproic Acid (VI). (a) From 2-Propionyl-6-methoxynaphthalene (V).—The Stobbe condensation between 8.56 g. of the ketone V and 17.52 g. of dimethyl succinate was carried out following the method of Daub and Johnson[15] by heating a solution of these reactants at 50–58° in 60 ml. of benzene with 2.4 g. of sodium hydride and a few drops of methanol. After the evolution of gas had stopped, the mixture was acidified with acetic acid and diluted with ether. The half-ester was extracted from the organic solution with eight 50-ml. portions of 5% sodium bicarbonate solution. These aqueous extracts were combined, acidified with hydrochloric acid, and the precipitated oil was taken up in ether. The ether solution was dried over anhydrous sodium sulfate and evaporated, leaving 13.1 g. (yield practically quantitative) of crude oily half-ester containing a little solvent which gave no color test with ferric chloride solution indicating the absence of succinoyl succinate. A total of 0.3 g. of starting ketone was recovered from the benzene–ether solution after removal of the succinoyl succinate by thorough washing with 5% potassium hydroxide.

The above half-ester was dissolved in 80 ml. of methanol and hydrogenated in the presence of 0.4 g. of Adams platinum oxide catalyst at room temperature and an initial pressure of 41 p.s.i. Within three hours the reaction had become very slow, the calculated amount of hydrogen having been absorbed. The mixture was filtered, the filtrate concentrated to about 40 ml. and water added to the point of incipient cloudiness. The crystals obtained on cooling were separated and recrystallized from dilute methanol giving a total of 6.93 g. (52% based on ketone V employed) of the half-ester VI, m. p. 142–145°, which was of sufficient purity for the cyclization described below. This product did not exhibit a depression of the melting point on admixture with the analytical specimen described below. Further crystals have not yet been obtained from the mother liquors.

(b) **By Selective Saponification of the Dimethyl Ester.**—A sample of 3-carboxy-4-(6-methoxy-2-naphthyl)-caproic acid,[4] m. p. 163–165°, was esterified with excess diazomethane in ether giving the dimethyl ester, as a colorless glass after evaporative distillation at 140° (0.25 mm.).

Anal. Calcd. for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.74; H, 7.17.

A 7.2-g. sample of this dimethyl ester was partially saponified with 3.3 g. of barium hydroxide octahydrate, 93 ml. of methanol and 62 ml. of water.[16] After refluxing for 6 hours the mixture was cooled, the precipitated barium salt removed by filtration and washed with ether. Acidification of the salt with cold dilute hydrochloric acid liberated the organic acid which was taken up in ethyl acetate. The oily residue obtained upon evaporation of the solvent was crystallized from dilute methanol yielding 3.2 g. of VI, m. p. 147–148°. An additional 1.2 g., m. p. 144–146°, was isolated from the original dilute alcoholic filtrate by concentration, washing with ether to remove neutral material, acidification, and recrystallization of the liberated organic acid. A sample of material recrystallized three times from dilute methanol was obtained as small colorless plates, m. p. 147–148°.

Anal. Calcd. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 68.89; H, 6.96.

Cyclization of 3-Carbomethoxy-4-(6-methoxy-2-naphthyl)-caproic Acid.—A cool solution of 0.330 g. of the half-ester VI, m. p. 142–145°, in 10 ml. of dry ether was treated with 2 drops of pyridine and 0.4 ml. of thionyl chloride. The mixture was allowed to stand at < 10° for 2 hours with occasional swirling, then evaporated at reduced pressure (water-pump) at < 10°. Benzene (5 ml.) was added and the evaporation process repeated at < 10° leaving a sirupy residue which was finally dried at 0.5 mm. for 0.5 hour. This product was dissolved in 10 ml. of dry thiophene-free benzene, and the mixture cooled in an ice-bath until the benzene began to solidify. A solution of 0.4 ml. of anhydrous stannic chloride in 0.4 ml. of thiophene-free benzene was then added, and the mixture was shaken vigorously. A bright red complex formed rapidly. After standing for 15 minutes at 0° the suspension was treated with a mixture of ice and 2 ml. of concentrated hydrochloric acid, ether was added and the whole was shaken vigorously to decompose the complex. The organic layer was separated, washed with water, then with 5% potassium hydroxide solution and dried over anhydrous sodium sulfate. Evaporation of the solvents gave a crude solid which on crystallization from methanol afforded 0.210 g. (67.5% yield) of methyl 1-ethyl-4-keto-7-methoxy-1,2,3,4-tetrahydrophenanthrene-2-carboxylate (III, R = CH_3), m. p. 128–130°, undepressed on admixture with the sample of VII, m. p. 129–130°, previously described.[4] A second crop amounting to 0.035 g., m. p. 85–122°, was obtained from the mother liquor. A sample of the pure material was saponified with 20% methanolic potassium hydroxide, giving after repeated recrystallization from dilute methanol and from ethyl acetate the keto acid III (R = H), melting at 215.5–217.5°, alone or on admixture with an authentic specimen of III (R = H).[4]

The 2,4-dinitrophenylhydrazone of the keto ester III (R = CH_3) crystallized from ethyl acetate in the form of red plates, m. p. 274.2–275°.

Anal. Calcd. for $C_{25}H_{24}O_7N_4$: C, 60.96; H, 4.91. Found: C, 61.04; H, 4.87.

In another cyclization carried out just as described above except that the temperature during the preparation of the acid chloride was maintained at 23°, the yield of III (R = CH_3) was 0.200 g. (64%), m. p. 129–130°. The second crop fraction amounted to 0.030 g., m. p. 113–126°, and the third yielded after recrystallization from methanol, 0.004 g. of the benzhydrindone IV (R = CH_3), m. p. 105–106°, undepressed on admixture with the authentic material, m. p. 104–105°, reported previously.[4]

Results essentially paralleling those described above were obtained when phosphorus pentachloride was used to prepare the acid chloride. Thus from 0.330 g. of half-ester in 10 ml. of thiophene-free benzene and 0.260 g. of phosphorus pentachloride added in three portions at 0° there was obtained after standing for 45 minutes at 0° with frequent shaking followed by treatment with 0.4 ml. of stannic chloride in benzene and working up as described

(11) Turner, THIS JOURNAL, **72**, 4318 (1950).

(12) All melting points are corrected for stem exposure.

(13) Microanalyses were kindly performed by James Rigas, Brooklyn, and B. Buell and E. Shiner, University of Wisconsin.

(14) Ultraviolet absorption spectra were determined in 95% alcohol solution on a Beckman quartz spectrophotometer.

(15) Daub and Johnson, THIS JOURNAL, **72**, 501 (1950).

(16) *Cf.* Johnson and Goldman, *ibid.*, **66**, 1030 (1944) and ref. 4.

above, 0.210 g. (67.5% yield) of keto ester III (R = CH_3), m. p. 126–129°; 0.020 g. of an intermediate fraction, m. p. 103–126°; and a third crop from which 0.004 g. of the benzhydrindone IV (R = CH_3), m. p. 105–106° was isolated.

Increasing the proportion of phosphorus pentachloride to 0.410 g. did not appreciably alter the results. However, when the cyclization was performed as described directly above except that the treatment with phosphorus pentachloride was carried out by refluxing the solution for 1 hour, there was obtained from a double-quantity run 0.180 g. of keto ester III (R = CH_3), m. p. 125–128° 0.052 g. of less pure material, m. p. 118–126°; and 0.100 g. of the benzhydrindone IV (R = CH_3), m. p. 102–103.5°.

3-Carbomethoxy-4-(6-methoxy-2-naphthyl)-3-pentenoic Acid.—The Stobbe condensation between 111.0 g. of 2-acetyl-6-methoxynaphthalene[17] and 122.0 g. of dimethyl succinate was carried out according to a described procedure[4] using 23.8 g. of potassium and 1000 ml. of *t*-butyl alcohol. Potassium carbonate solution (5%) was employed for extracting the half-ester. Acidification of the alkaline extracts yielded an oily mixture of half-esters which was taken up in ether. Upon removal of a portion of the ether by distillation 40.0 g. of the half-ester crystallized, m. p. 150–153°. After recrystallization from ethyl acetate it was obtained as colorless plates, m. p. 160–162°.

Anal. Calcd. for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found: C, 68.58; H, 5.83.

α-3-Carbomethoxy-4-(6-methoxy-2-naphthyl)-valeric Acid.—A solution of 35.0 g. of the half-ester, m. p. 160–162°, in 200 ml. of methanol containing a few drops of acetic acid was hydrogenated over 2 g. of Adams platinum oxide catalyst at room temperature and 45 p.s.i. The calculated amount of gas was absorbed in 1 hour. The mixture was filtered, the filtrate evaporated and the residue crystallized from ether–pentane giving 25.0 g. of colorless product, m. p. 118–121°. Recrystallization from ether gave colorless prisms, m. p. 121–122°.

Anal. Calcd. for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.07; H, 6.30.

α-3-Carboxy-4-(6-methoxy-2-naphthyl)-valeric acid was prepared by saponification of 15.0 g. of the half-ester, m. p. 118–121°, of the preceding experiment with 100 ml. of methanol and 90 ml. of 20% potassium hydroxide. After refluxing for 1 hour, the methanol was removed by distillation and the solution cooled and acidified. The crystalline acid which precipitated amounted to 11.0 g., m. p. 147–152° (dec.). Recrystallization from ether afforded colorless rosettes, m. p. 158–160° (dec.).

Anal. Calcd. for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: 67.34; H, 6.08.

The α-dimethyl ester was prepared by the action of ethereal diazomethane on the α-half-ester. It crystallized from alcohol in the form of colorless prismatic aggregates, m. p. 57–59°.

Anal. Calcd. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.17; H, 6.60.

β-3-Carboxy-4-(6-methoxy-2-naphthyl)-valeric Acid.—The oily unsaturated half-ester remaining upon evaporation of the mother liquor of the crystalline Stobbe condensation product (see above) was dissolved in 200 ml. of methanol and hydrogenated over 2 g. of Adams platinum oxide catalyst at room temperature and 45 p.s.i., until gas absorption ceased (3 days). About 70% of the calculated amount of hydrogen reacted. Acetone was added to dissolve material which crystallized from solution during the reduction, and the mixture was filtered. The residue obtained on evaporation of the solvent was crystallized from methanol yielding 40.0 g. of crude half-ester, m. p. 150–158°. Recrystallization did not raise the m. p., so the product was saponified by refluxing for 1 hour with 150 ml. of methanol and 40 ml. of 45% potassium hydroxide. The crude dibasic acid obtained on dilution and acidification amounted to 37.0 g., m. p. 166–179° (dec.). Recrystallization from ether gave small colorless plates, m. p. 188–190° when inserted at 180°. On admixture with the α-isomer, the m. p. was 140–161°.

Anal. Calcd. for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.26; H, 6.02.

Esterification of the β-dibasic acid by the method of Clinton and Laskowski[18] gave the β-dimethyl ester which crystallized from alcohol in the form of colorless plates, m. p. 88–90°.

Anal. Calcd. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.10; H, 6.65.

β-3-Carbomethoxy-4-(6-methoxy-2-naphthyl)-valeric Acid.—To a hot solution of 12.95 g. of the β-dimethyl ester, m. p. 88–90°, in 100 ml. of methanol was added 39.2 ml. of 1 *N* NaOH dropwise with stirring. After refluxing for one-half hour the mixture was diluted with water, washed with ether to remove neutral material, and acidified. The organic acid which precipitated was recrystallized from ethyl acetate to give 8.00 g. of the β-half-ester in the form of colorless plates, m. p. 160–162°.

Anal. Calcd. for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.84; H, 6.35.

Methyl 1-Methyl-4-keto-7-methoxy-1,2,3,4-tetrahydrophenanthrene-2-carboxylate (α-Form).—To a cooled solution of 2.5 ml. of dry ether containing 1 drop of pyridine was added 1 ml. of purified[19] thionyl chloride, followed by 1.90 g. of the α-half-ester, m. p. 118–121°, described above. The acid was dissolved by swirling, and the mixture was allowed to stand at 25° for one-half hour. The solvent and excess thionyl chloride was removed *in vacuo*, the temperature never exceeding 40°; then a few milliliters of dry benzene was added and the concentration process repeated followed by evacuation at < 1 mm. with warming at 40°. The oily residue was dissolved in 10 ml. of dry thiophene-free benzene, cooled to 5°, and then a solution of 2 ml. of anhydrous stannic chloride in 2 ml. of benzene was added. The mixture containing a red insoluble complex was swirled at 5° for ten minutes, then treated with a mixture of ice and 50 ml. of concentrated hydrochloric acid. Ether was added, and the organic layer was separated, washed with 10% hydrochloric acid, then with saturated sodium bicarbonate, and dried over anhydrous sodium sulfate. The residue obtained on evaporation of the ether was crystallized from methanol giving 1.20 g. (67% yield) of faintly yellow elongated hexagonal plates, m. p. 110–111°; λ_{max} 220 mμ (log *E* 4.86), 247 (4.60), 315 (3.87), 345 (3.57).[14]

Anal. Calcd. for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.62; H, 6.20.

This substance was recovered unchanged after refluxing for 3 hours in pyridine–ethanol with semicarbazide hydrochloride.

The 2,4-dinitrophenylhydrazone was formed in the usual manner[20] by heating for one-half hour. Because of its sparing solubility a satisfactory solvent for recrystallization was not found. The derivative, m. p. 248–250° (dec.), was prepared for analysis by washing thoroughly with hot alcohol and ethyl acetate.

Anal. Calcd. for $C_{24}H_{22}O_7N_4$: C, 60.24; H, 4.64. Found: C, 60.13; H, 4.50.

Methyl 1-Methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene-2-carboxylate (α-Form).—A mixture of 1.20 g. of the keto ester (α-form), m. p. 110–111°, described in the preceding experiment, 0.3 g. of 30% palladium-on-carbon,[21] 50 ml. of acetic acid and 2 ml. of 60% perchloric

(17) Prepared by the method of Robinson and Rydon, *J. Chem. Soc.*, 1394 (1939).

(18) Clinton and Laskowski, THIS JOURNAL, **70**, 3135 (1948).

(19) Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 381.

(20) Allen, THIS JOURNAL, **52**, 2955 (1930).

(21) Prepared by method B of Mozingo, *Org. Syn.*, **26**, 77 (1946), with additional palladium to make 30%.

acid[22] was shaken with hydrogen at 58 p.s.i. for 24 hours at room temperature. The mixture was diluted with water, extracted with ether, the ether solution was washed with saturated sodium bicarbonate and dried over anhydrous sodium sulfate. The product remaining on distilling off the ether was crystallized from methanol to give 0.20 g. of colorless rods, m. p. 115–116.5°.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.07, H, 7.05.

Dehydrogenation of 0.18 g. of the above α-ester (m. p. 115–116.5°) was effected by heating under nitrogen at 350° with 0.18 g. of 30% palladium-on-carbon[21] for twenty minutes. The product was treated with acetone, filtered and the filtrate evaporated. The residue was refluxed with 10 ml. of ethanol and 1 ml. of 45% potassium hydroxide for one hour, diluted with water and extracted with ether. The ether solution was washed with water and dried over anhydrous sodium sulfate. The residue left on distillation of the ether was crystallized from methanol to give 0.02 g. of material, m. p. 127–129°, undepressed on admixture with an authentic specimen of 1-methyl-7-methoxyphenanthrene, m. p. 132.5–133.5°.[9]

Anal. Calcd. for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.25; H, 6.37.

This product formed a yellow *sym*-trinitrobenzene derivative which was crystallized from alcohol, m. p. 137–139°, undepressed on admixture with an authentic specimen of the trinitrobenzene derivative of 1-methyl-7-methoxyphenanthrene, m. p. 139–141°.[9]

Methyl 1-Methyl-4-keto-7-methoxy-1,2,3,4-tetrahydrophenanthrene-2-carboxylate (β-Form).—The cyclization of 5.00 g. of the β-half-ester, m. p. 158–160°, was carried out by the procedure described above for the α-stereoisomer, the amounts of reagents being increased proportionately. The keto ester which crystallized from methanol amounted to 3.50 g. (73% yield), m. p. 110–111°. Recrystallization gave colorless elongated hexagonal plates, m. p. 114–115.5°; λ_{max} 220 mμ (log E 4.77), 247 (4.47), 315 (3.91), 345 (3.59).[14]

Anal. Calcd. for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.57; H, 6.19.

The semicarbazone was formed in about 50% yield by refluxing the keto ester in pyridine–ethanol with semicarbazide hydrochloride for 3.5 hours. It crystallized from ethyl acetate in the form of pale yellow plates, m. p. 207–210° (dec.).

Anal. Calcd. for $C_{19}H_{21}O_4N_3$: C, 64.21; H, 5.96. Found: C, 64.25; H, 5.93.

Saponification of the keto ester with alcoholic potassium hydroxide yielded **1-methyl-4-keto-7-methoxy-1,2,3,4-tetrahydrophenanthrene-2-carboxylic acid,** which crystallized from ethyl acetate in the form of colorless prism clusters, m. p. 228–230°.

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.98; H, 5.62.

Methyl 1-Methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene-2-carboxylate (β-Form).—The keto ester described in the preceding experiment was hydrogenated by a modification of the method of Zelinsky, Packendorff and Leder-Packendorff.[23] A suspension of 1 g. of Adams platinum oxide catalyst in 100 ml. of methanol was reduced with hydrogen, and a 6-g. sample of the keto ester, m. p. 110–112°, was then added followed by 0.5 ml. of a commercial palladium chloride solution[24] containing 0.05 g. of palladium. This mixture was shaken at room temperature with hydrogen at 58 p.s.i., and the calculated amount of gas was absorbed in a few minutes. Acetone was added to the gelatinous crystalline mixture in order to effect solution. After filtration to remove catalyst and evaporation, the residue (6.0 g., m. p. 98–106°) was recrystallized from methanol and from ethyl acetate–pentane giving small colorless needles, m. p. 109–111°, (reported,[10] 110–112°); yield 60%. On admixture with the α-isomer described above the m. p. was 97–102°.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.83; H, 6.94.

Saponification with alcoholic potassium hydroxide gave **1-methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene-2-carboxylic acid.** Recrystallized from methanol and from ethyl acetate–cyclohexane it was obtained as colorless needles, m. p. 197–200° (reported,[10] 203–204°).

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.72. Found: C, 75.34; H, 6.64.

Dehydrogenation of the β-ester described in the preceding experiment as described above for the α-ester yielded a product which gave a *sym*-trinitrobenzene derivative, m. p. 136–139°, undepressed on admixture with an authentic specimen of the trinitrobenzene derivative of 1-methyl-7-methoxyphenanthrene, m. p. 139–141°.[9] Our derivative also had a carbon and hydrogen content in agreement with this formula.

Dehydrogenation under mild conditions resulted in retention of the carbomethoxy group. Thus when 0.80 g. of the β-ester was heated under nitrogen at 250° with 0.80 g. of 30% palladium-on-carbon[21] for 8 minutes, the product treated with acetone, filtered and the filtrate evaporated, there was obtained after recrystallization from methanol 0.50 g. of methyl 1-methyl-7-methoxyphenanthrene-2-carboxylate, m. p. 188–189° (reported,[10] 184–186°).

Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.30; H, 5.69.

Saponification of the dehydrogenated ester with alcoholic potassium hydroxide gave the free acid. Recrystallization from methanol gave a colorless product, m. p. 288–290° (reported,[10] 288–290°).

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30. Found: C, 76.70; H, 5.39.

3-Carbomethoxy-4-(5,6,7,8-tetrahydro-2-naphthyl)-valeric Acid (IX).—To a solution of 8.0 g. of the dimethyl ester corresponding to IX[11] in 50 ml. of methanol was added 26 ml. of 1 *N* NaOH. After refluxing for 20 minutes, the solution was diluted with 100 ml. of water, washed with ether and acidified. The precipitated acid was recrystallized from acetone–ether giving 7.0 g. of colorless plates, m. p. 142–144°.

Anal. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.25; H, 7.61.

Methyl 1-Methyl-4-keto-1,2,3,4,5,6,7,8-octahydroanthracene-2-carboxylate (X).—The half-ester (6.0 g.) described in the preceding experiment was cyclized by the thionyl chloride–stannic chloride method described above for the α-half ester. The neutral product was crystallized from ethanol, yielding 4.4 g. of X as colorless rods, m. p. 102–103.5°, undepressed on admixture with an authentic specimen.[11]

Summary

The previously described synthesis of bisdehydrodoisynolic acid,[4] which yields at the cyclization step a preponderance of the product of five- instead of the required six-membered ring closure, has been markedly improved. It has now been found that ring closure occurs predominantly in the desired manner if the acid chloride of the half-ester VI is employed instead of the anhydride II. The product is the keto ester III (R = CH_3) which can be employed directly in the subsequent steps of the synthesis and an esterification step is thus eliminated. This improvement coupled with the fact that the half-ester can be prepared directly by hydrogenation of the crude Stobbe

(22) *Cf.* Rosenmund and Karg, *Ber.*, **75**, 1850 (1942).

(23) Zelinsky, Packendorff and Leder-Packendorff, *ibid.*, **66**, 872 (1932); **67**, 300 (1934).

(24) Supplied by J. Bishop Co., Malvern, Pa. See Alexander and Cope, *Org. Syn.*, **26**, 31 (1946).

condensation product from 2-propionyl-6-methoxynaphthalene (V) and dimethyl succinate, reduces the total number of steps of the synthesis to *seven* starting with β-methoxynaphthalene.

A similar cyclization study has been made also with the lower homolog VI (CH_3 in place of C_2H_5) which was obtained in two diastereoisomeric forms. The stereochemical integrity was retained throughout both the cyclization step to give two forms of the keto ester, and the reduction step affording two stereoisomeric forms of VII (CH_3 in place of C_2H_5). The structure of these products was shown by dehydrogenation experiments.

The cyclization method was also extended to the tetrahydro half-ester IX which gave the expected product of linear cyclization, namely, X.

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Spectrophotometric Studies of Cobalt(II) Thiocyanate Complexes in Organic Solvents

BY LEONARD I. KATZIN AND ELIZABETH GEBERT

Cobaltous nitrate dissolved in organic solvents gives a red to magenta solution, due to formation of undissociated cobaltous nitrate.[1] Addition of lithium nitrate or tetrabutylammonium nitrate to the solution in acetone, or tetrabutylammonium nitrate to the solution in *t*-butyl alcohol, gives a trinitrate complex which in the alcohol, at least, is relatively weak.[1] Cobalt chloride dissolved in most organic solvents gives an intense blue color, apparently associated with formation of entities corresponding to CoX_2Cl_2, where X represents a solvent molecule.[2] With a weak electron donor such as acetone or tetrahydrofuran as the solvent, addition of lithium chloride gives a series of forms, $CoXCl_3^-$ and $CoCl_4^=$ with characteristic absorptions. In alcohol solutions, $CoCl_4^=$ is apparently unobtainable, and the $CoXCl_3^-$ achieved only with difficulty. Both anion and solvent effects are therefore identifiable.

The thiocyanate complex of cobalt(II) is rather stable, from the criterion of formation of salts with $Co(SCN)_4^=$ groupings, etc., in comparison with the other complexes mentioned. These salts are blue, as are solutions of cobalt with thiocyanate in organic solvents. The comparison of spectra and complexes with those of the nitrate and chloride salts is therefore of interest.

Procedures

Spectrophotometric measurements were made with the Beckman model DU quartz spectrophotometer. The density scale of the instrument was calibrated with standards obtained from the National Bureau of Standards. Density settings were found reproducible to 0.002 density unit.

Cobalt perchlorate was prepared from the carbonate and perchloric acid, and recrystallized twice. The solid so obtained was the hexahydrate. Lithium thiocyanate was prepared in acetone solution by metathesis of potassium thiocyanate and lithium nitrate in acetone solution. The precipitated potassium nitrate was removed by centrifugation, and the thiocyanate concentration checked by titration against a silver nitrate standard. The preparation of the lithium salt was advisable, to avoid precipitation of potassium perchlorate on mixing with the cobalt solutions. The thiocyanate solution is colorless.

Solvents used were the commercial pure products. Stock solutions were made of the salts in the desired solvents, and aliquot dilutions made for spectrophotometric study. Cobalt concentrations were determined for the stocks by standard electrodeposition procedures. Pyridine solutions were made from weighed portions of the liquid. Thiocyanate solution preparation and standardization has been described above.

Experimental

Job[3] has described a procedure for determining the formula of an additive complex which he has called the method of continuous variations, and which we have extended to the case of formation of more than one complex.[1,4] In brief, when stocks of the two reagents, of equal concentration, are mixed in various proportions, the concentration of the complex is at a maximum when the reagents are in the ratio of their stoichiometric proportions in the complex. When more than one complex is formed,[1] the lowest complex is at a maximum at a reactant ratio less than the stoichiometric, the highest complex is a maximum at a ratio greater than the stoichiometric, and the direction and extent of deviation of any intermediate complex from the stoichiometric maximum depends in detail on the system. When changes in the absorption of the mixtures are used to measure the concentrations of the complexes, the maxima in the absorption changes will in general not fall at the maxima in the complex concentrations, except when a wave length is chosen at which the absorption is ascribable almost solely to a single complex. Otherwise there may be one, two or three maxima and/or minima in the deviation plot; for details one is referred to the original.[1]

On applying this technique to mixtures of cobalt perchlorate and lithium thiocyanate in acetone, one finds, on plotting the excess optical density over that of the components against the thiocyanate formal concentration (Fig. 1), that one is dealing with both a trithiocyanate and a tetrathiocyanate complex. The wave lengths chosen for Fig. 1 were based on a plot (Fig. 2) of logarithm of

(1) L. I. Katzin and E. Gebert, THIS JOURNAL, **72**, 5455 (1950).
(2) L. I. Katzin and E. Gebert, *ibid.*, **72**, 5466 (1950).
(3) P. Job, *Ann. chim.*, [10] **9**, 113-134 (1928).
(4) W. C. Vosburgh and G. R. Cooper, THIS JOURNAL, **63**, 437 (1941).