dehyde *o*-formylphenylhydrazone, m.p. 157–158°. Other experiments gave yields varying from 86 to 93%.

(b) **From the Ethylene Acetal.**—Following the procedure described in (a) 0.65 g. (0.0028 mole) of nitroformaldehyde *o*-formylphenylhydrazone ethylene acetal was hydrolyzed with 2 ml. of concentrated hydrochloric acid in 150 ml. of hot water, giving, after extraction and recrystallization, 0.49 g. (94%) of nitroformaldehyde *o*-formylphenylhydrazone, m.p. 157–158°.

3-Nitrocinnoline (IVa).—A Witt plate of the appropriate diameter was placed on the wall indentations (A) of the apparatus shown in the scale drawing (Fig. 1). The plate provided a platform for 6 g. of dry ion exchange resin, Amberlite IRA-400.[10] With heating to 55° by means of the Nichrome coil (B), a solution of 2.0 g. (0.01 mole) of nitroformaldehyde *o*-formylphenylhydrazone in 300 ml. of tetrahydrofuran was circulated through the apparatus for 18 hr. by means of the propeller stirring rod (C).[21] The two outlets (E) and (F) were fitted with a ball-joint stirrer sleeve[22] and a reflux condenser, respectively. The solution was filtered and the solvent was removed by distillation on the steam-bath. The light tan solid was recrystallized from dilute acetone (charcoal), giving 1.0 g. (55%) of 3-nitrocinnoline, m.p. 204–205°.

In several experiments the solution was refluxed over the resin in the usual reflux set-up using either tetrahydrofuran or dimethoxyethane as the solvent for periods varying from 10 to 20 hr. The reflux procedure gave yields about 10% lower and the resin underwent partial decomposition. When the quantity of resin used was lowered to 3 g., only a trace of 3-nitrocinnoline could be isolated. Raising the quantity of resin used did not effect any increase in the yield.

(21) A spiral impeller, such as described by H. E. Drechsel (*Anal. Chem.*, **29**, 659 (1957)), might be preferable.

(22) Organic Chemical Bulletin (Eastman Kodak Co.), **24**, no. 3 (1952).

LINCOLN 8, NEBRASKA

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

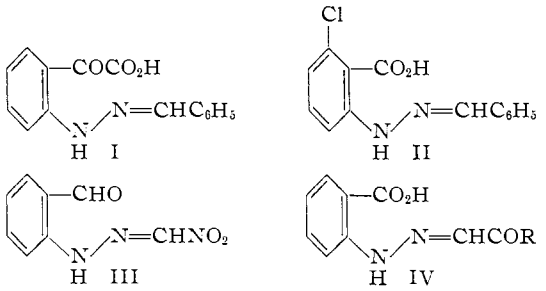
Cinnolines. IV. Synthesis of 3-Acetyl- and 3-Carbethoxycinnolines[1,2]

BY HENRY E. BAUMGARTEN AND CHARLES H. ANDERSON

RECEIVED NOVEMBER 8, 1957

Diazotization of *o*-aminobenzaldehyde and coupling of the diazonium salt with acetoacetic acid gave the unstable pyruvaldehyde 1-(*o*-formylphenylhydrazone) (VIa), which cyclized spontaneously to form 3-acetylcinnoline. Coupling of the diazonium salt with ethyl hydrogen malonate and spontaneous cyclization of the unstable ethyl glyoxalate *o*-formylphenylhydrazone (VIIIa) gave 3-carbethoxycinnoline. In a somewhat similar fashion 2-amino-4-chloro- and 2-amino-5-chlorobenzaldehydes gave the corresponding 3-acetyl-7-chloro- and 3-acetyl-6-chlorocinnoline and the 3-carbethoxy-7-chloro- and 3-carbethoxy-6-chlorocinnoline, respectively, although the cyclization step was not always both spontaneous and complete in these examples.

Three related syntheses of the cinnoline ring system have employed the cyclization of an *o*-acyl- or *o*-carboxyphenylhydrazone (I-III) in the terminal step: the Stolle–Becker[3] synthesis (I), the Pfannstiehl–Janecke[4] synthesis (II) and that (III) reported from this Laboratory.[1,5] Each of the first two of these procedures is known by a single example, and an attempt by Leonard, Boyd and Herbrandson[6] to extend the Pfannstiehl–Janecke synthesis to phenylhydrazones of the type IV was not successful. In the first paper[5] of this series it was suggested that the cyclization of derivatives of IV in which the carboxyl group was replaced by formyl or acetyl might be more satisfactory than the cyclization of IV itself. This possibility has now been realized in part and is the subject of this communication.



When *o*-aminobenzaldehyde (Va)[7] was diazotized and coupled with acetoacetic acid, the expected pyruvaldehyde 1-(*o*-formylphenylhydrazone) (VIa) appeared to form, but purification of the product yielded only the cyclized 3-acetylcinnoline (VIIa) in 16–22% yield. Although cyclization may have occurred in some experiments during the recrystallization of the product, in others examination of the crude material indicated that cyclization had occurred at some earlier stage, and thus far no authentic sample of VIa has been obtained. The identity of VIIa was established by analysis, comparison of its infrared spectrum with that of the presumably analogous 3-acetylquinoline and conversion of VIIa into the known 3-aminocinnoline[5] by application of the Schmidt reaction.

When Va was diazotized and coupled with ethyl hydrogen malonate, the product was a tarry material from which only 3-carbethoxycinnoline (IXa) could be isolated in 8–12% yield. The assignment of structure was based upon analysis and the infrared spectrum. Again none of the intermediate ethyl glyoxylate *o*-formylphenylhydrazone (VIIIa) has been isolated.

Extension of the above operations to 2-amino-4-chlorobenzaldehyde[7] (Vb) and to 2-amino-5-chlorobenzaldehyde[7] (Vc) gave somewhat different re-

(1) Paper III, THIS JOURNAL, **80**, 1977 (1958).

(2) This work was supported in part by grant G-1090 of the National Science Foundation.

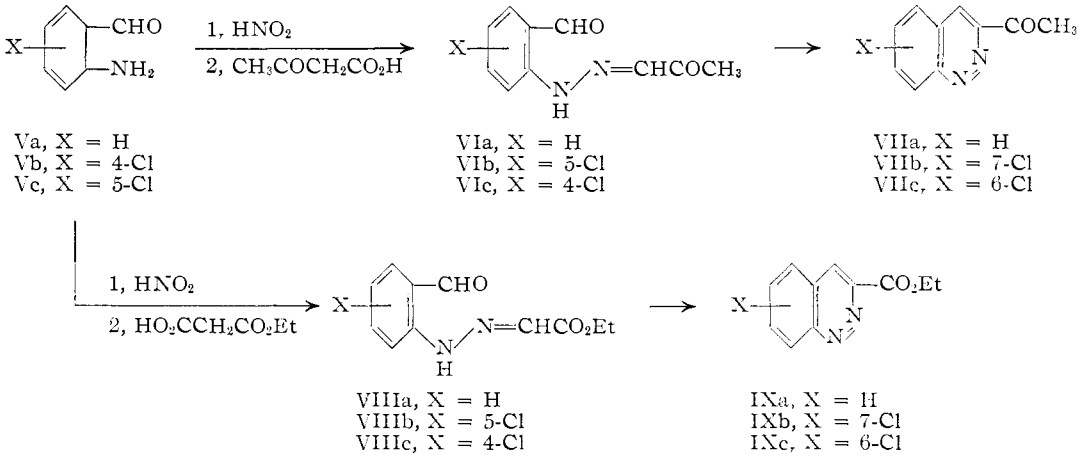
(3) R. Stolle and W. Becker, *Ber.*, **57**, 1123 (1924).

(4) K. Pfannstiehl and J. Janecke, *ibid.*, **75B**, 1096 (1942).

(5) H. E. Baumgarten and M. R. DeBrunner, THIS JOURNAL, **76**, 3489 (1954).

(6) N. J. Leonard, S. N. Boyd, Jr., and H. F. Herbrandson, *J. Org. Chem.*, **12**, 47 (1947).

(7) The o-aminobenzaldehydes used in this study were prepared from the corresponding o-nitrobenzaldehydes as described previously[1,5] and were crude materials. Over-all yields are based, therefore, on the o-nitrobenzaldehyde.



Va, X = H
Vb, X = 4-Cl
Vc, X = 5-Cl

VIa, X = H
VIb, X = 5-Cl
VIc, X = 4-Cl

VIIa, X = H
VIIb, X = 7-Cl
VIIc, X = 6-Cl

VIIIa, X = H
VIIIb, X = 5-Cl
VIIIc, X = 4-Cl

IXa, X = H
IXb, X = 7-Cl
IXc, X = 6-Cl

sults. From diazotized Vc and acetoacetic acid only the cyclized product, 3-acetyl-6-chlorocinnoline (VIIc), could be obtained as analytically pure material (in 17% yield). However, partially purified material exhibited an infrared spectrum to be expected of a mixture of pyruvaldehyde 1-(4-chloro-2-formylphenylhydrazone) (VIc) as the major component with a small amount of VIIc. The cyclization appeared to take place principally during recrystallization and appeared to be aided by traces of mineral acid.[8] From diazotized Vc and ethyl hydrogen malonate either the cyclized product, 3-carbethoxy-6-chlorocinnoline (IXc), or an apparent mixture of IXc and ethyl glyoxalate 4-chloro-2-formylphenylhydrazone (VIIIc) could be obtained, although the yield of IXc was quite low (5%). Here also the presence of traces of mineral acid during recrystallization appeared to facilitate cyclization.

When Vb was diazotized and coupled with acetoacetic acid a product consisting largely of uncyclized pyruvaldehyde 1-(5-chloro-2-formylphenylhydrazone) (VIb) was obtained in 18% yield. Cyclization of VIb was effected by treatment with 20% hydrochloric acid (under which conditions conversion was incomplete) or, preferably, with concentrated sulfuric acid, the latter treatment giving a 39% yield of 3-acetyl-7-chlorocinnoline (VIIb). Attempted thermal and base-catalyzed cyclizations of VIb were ineffective. From diazotized Vb and ethyl hydrogen malonate the uncyclized ethyl glyoxylate 5-chloro-2-formylphenylhydrazone (VIIIb) was obtained in 6% yield; however, when the process was repeated to obtain a larger amount of material for cyclization experiments, the product was a mixture of VIIIb and 3-carbethoxy-7-chlorocinnoline (IXb) from which IXb was isolated in about 1% yield. Acid-catalyzed cyclization of VIIIb in aqueous mineral acid has not been satisfactory thus far, possibly because of competitive hydrolytic reactions.

(8) This conclusion is based on the following observation. After recrystallization proved to be relatively ineffective in the separation of VIc and VIIc, an attempt was made to extract the mixture with 10% hydrochloric acid. Although almost no acid-soluble material was obtained, recrystallization of the acid-insoluble fraction yielded VIIc free from VIc. The alternative explanation that the acid treatment simply destroyed the VIc present is less attractive, for the infrared spectrum of the original mixture indicated that there was much less VIIc present than was ultimately obtained.

Because of the sometimes erratic nature of the ring closure step it was convenient to follow the course of cyclization by use of infrared spectra run on the crude products at each state of treatment or purification. A detailed discussion of the spectra must await the conclusion of an extensive study of model compounds now in progress and will be published later in this series; however, for the purpose at hand it is fortunate that there were several spectral features that facilitated the determination of the extent of cyclization in the products. Considering first the uncyclized intermediates VI and VIII in carbon tetrachloride solution there was a single weak band appearing at 3240–3186 cm.$^{-1}$ characteristic of the bonded ν (N–H) vibration. In the Nujol mull the position of the band was 0 to 40 cm.$^{-1}$ lower in frequency. In solutions of VI (but not in the mull) the two weak bands characteristic of the normal (not bonded through the C–H bond) formyl group[9] appeared at 2740–2735 cm.$^{-1}$ and 2840–2835 cm.$^{-1}$ There were two to four bands in the 1720–1610 (ν (C=O)) cm.$^{-1}$ region. Perhaps the most striking and useful bands were the three medium to strong bands appearing at 1609–1598, 1573–1562 and 1520–1508 cm.$^{-1}$ in the mull spectra[10] of both VI and VIII and a fourth band at 1597–1583 cm.$^{-1}$ in the spectra of VI. Upon cyclization the ν(N–H) band, the formyl bands and all but one[11] of the ν (C=O) bands disappeared. The three or four bands in the 1610–1510 cm.$^{-1}$ region were replaced by a single weak band at 1617–1607 cm.$^{-1}$. This last change was the most useful for following the course of cyclization and was used also as a measure of purity of the cyclized products.

The tendency of the intermediates VI and VIII to cyclize was further emphasized by their spectra. Although some of these substances were obtained in a state of purity within the usual analytical limits, they were not obtained in the spectroscopically pure state. The spectrum of each of these substances indicated the presence of a minute amount of the corresponding cyclized product.

(9) S. Pinchas, *Anal. Chem.*, **29**, 334 (1957).

(10) These bands fall in one of the regions of strong absorption by carbon tetrachloride and are not readily observed in such solutions.

(11) The solution spectra of IX show a second weak band in the carbonyl region at about 30 cm.$^{-1}$ higher than the main ester carbonyl band. The origin of this weaker band is being studied.

Experimental[12]

3-Acetylcinnoline (VIIa).—To a solution of 7.7 g. (0.13 mole) of potassium hydroxide in 200 ml. of water was added with stirring 15.5 g. (15 ml., 0.12 mole) of ethyl acetoacetate. The mixture was stirred for four hours and then allowed to stand for 20 hr.

A mixture of 14 g. (0.12 mole maximum) of damp, crude *o*-aminobenzaldehyde (from 0.13 mole of *o*-nitrobenzaldehyde[13]), 8.3 g. (0.12 mole) of sodium nitrite and 250 ml. of ice-water was made into a slurry in the Waring blender. To this slurry was added in one portion a mixture of 25 ml. (0.3 mole) of concentrated hydrochloric acid and 150 g. of crushed ice. The mixture was blended for about five minutes. Small amounts of crushed ice were added periodically during blending. The solution was filtered.

The solution of potassium acetoacetate was cooled to 0° and 15 ml. of concentrated hydrochloric acid in 35 ml. of water was added slowly with stirring.[14] The diazonium salt solution was added over a period of 15 min. and the mixture was neutralized (to congo red paper) by addition of sodium acetate. The yellow solid, which formed slowly, turned dark orange upon standing at room temperature for two hours. The solid was collected on a filter and recrystallized from 25% ethanol or, preferably, Skellysolve C,[15] giving 3.7 g. (16%, based on *o*-nitrobenzaldehyde) of 3-acetylcinnoline as pale yellow needles, m.p. 155–156°. Other experiments gave crude yields up to 40%, yields of purified material up to 22%.

Anal. Calcd. for $C_{10}H_8N_2O$: C, 69.75; H, 4.68; N, 16.27. Found: C, 69.50; H, 4.72; N, 16.28.

3-Aminocinnoline.—To a solution of 1 g. (0.006 mole) of 3-acetylcinnoline in 6 ml. of concentrated sulfuric acid (cooled to room temperature) was added 0.4 g. of sodium azide in small portions. After each addition, the solution foamed vigorously. The addition required about one hour. The mixture was allowed to stand overnight. It was poured with stirring onto 12 g. of chipped ice and the resulting solution was heated on the steam-bath for 15 hr. The solution was neutralized with 33% aqueous potassium hydroxide and the yellow precipitate that formed was collected by filtration. The filtrate was extracted with ether. The ether was evaporated and the residue was combined with the yellow precipitate and recrystallized from hot benzene, giving 0.08 g. (10%) of 3-aminocinnoline, m.p. 163–164.5°. The infrared spectrum, m.p. and mixed m.p. were identical with those of an authentic sample of 3-aminocinnoline.[5] Another experiment gave a 15% yield of 3-aminocinnoline.

3-Carbethoxycinnoline (IXa).—A solution of the diazonium salt was prepared from 20 g. (0.15 mole maximum) of damp, crude *o*-aminobenzaldehyde (from 0.20 mole of *o*-nitrobenzaldehyde[13]), 14.2 g. (0.21 mole) of sodium nitrite, 250 ml. of ice-water, 42 ml. (0.5 mole) of concentrated hydrochloric acid and 150 g. of crushed ice in the Waring blender as described in the preparation of 3-acetylcinnoline.

The diazonium salt solution was added over a period of 15 min. to a cold solution of 34 g. (0.20 mole) of the monopotassium salt of ethyl hydrogen malonate[16] in 400 ml. of water which had been cooled to 0° in an ice-bath and neutralized by the slow addition of 25 ml. of concentrated hydrochloric acid in 50 ml. of water. The mixture was neutralized (to congo red) by addition of sodium acetate and was allowed to warm up to room temperature over a period of two hours. The mixture was heated to 60° on the steam-bath, during which heating a brown tar formed. After being cooled the solution was decanted from the tar and extracted with ether. The oil obtained by evaporation of the ether was combined with the tar, and the resultant mixture was heated under reflux with Skellysolve B[17] and filtered. Upon cooling long yellow needles of 3-carbethoxycinnoline, m.p. 97–97.5°, 3.4 g. (8%, based on *o*-nitrobenzaldehyde), precipitated. Other experiments gave yields up to 12%.

Anal. Calcd. for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98; N, 13.86. Found: C, 65.29; H, 5.03; N, 13.75.

3-Acetyl-6-chlorocinnoline (VIIc).—The diazonium salt solution, prepared as described in the preparation of 3-acetylcinnoline from 18 g. (0.1 mole maximum) of damp, crude 2-amino-5-chlorobenzaldehyde (from 0.17 mole of 5-chloro-2-nitrobenzaldehyde[1]), 11.6 g. (0.17 mole) of sodium nitrite, 250 ml. of ice-water, 35 ml. (0.42 mole) of concentrated hydrochloric acid and 150 g. of crushed ice, was added over a period of 15 min. to an aqueous solution of acetoacetic acid[14] (prepared from 0.17 mole of ethyl acetoacetate). The mixture was neutralized (to congo red) by addition of sodium acetate and heated to 75°. After cooling the solution, the solids formed were collected and recrystallized several times from Skellysolve C,[15] giving 7 g. (*ca.* 21%) of crude pyruvaldehyde 1-(4-chloro-2-formylphenylhydrazone), m.p. 143–175°. The infrared spectrum of this material showed it to be largely the compound cited contaminated with a small amount of 3-acetyl-6-chlorocinnoline. The crude material was washed with 10% hydrochloric acid. The acid-insoluble residue was dried and recrystallized several times from Skellysolve C,[15] giving 6.0 g. (18%, based on 5-chloro-2-nitrobenzaldehyde) of 3-acetyl-6-chlorocinnoline, m.p. 206–207°.

Anal. Calcd. for $C_{10}H_7N_2OCl$: C, 58.13; H, 3.42; N, 13.55; Cl, 17.16. Found: C, 58.36; H, 3.57; N, 13.65; Cl, 17.41.

3-Carbethoxy-6-chlorocinnoline (IXc).—The diazonium salt solution, prepared as in the preceding preparation, was added over a period of 15 min. to an aqueous solution of 0.17 mole of ethyl hydrogen malonate (*vide supra*) cooled to 0° in an ice-bath. The mixture was neutralized (to congo red) by addition of sodium acetate and was heated to 75°. After cooling the solution, the solids formed were collected and recrystallized from Skellysolve C, giving 3.8 g. of mixed crystals, m.p. 124–128° (with a few particles melting at 144°). The infrared spectrum of the product indicated it to be a mixture consisting largely of ethyl glyoxalate 4-chloro-2-formylphenylhydrazone with a smaller amount of 3-carbethoxy-6-chlorocinnoline. The crystals were washed with 10% hydrochloric acid and recrystallized several times from Skellysolve C,[15] giving 2 g. (5%, based on 5-chloro-2-nitrobenzaldehyde) of 3-carbethoxy-6-chlorocinnoline, as long yellow needles, m.p. 152.5–153°.

Anal. Calcd. for $C_{11}H_9N_2O_2Cl$: C, 55.82; H, 3.83; N, 11.81; Cl, 14.98. Found: C, 55.57; H, 3.77; N, 11.52; Cl, 15.17.

Pyruvaldehyde 1-(5-Chloro-2-formylphenylhydrazone) (VIb).—The diazonium salt solution, prepared as described above in the preparation of 3-acetylcinnoline from the damp, crude 2-amino-4-chlorobenzaldehyde (from 0.15 mole of 4-chloro-2-nitrobenzaldehyde[1]), 10.4 g. (0.15 mole) of sodium nitrite, 250 ml. of ice-water, 32 ml. (0.38 mole) of concentrated hydrochloric acid and 150 g. of crushed ice, was added over a period of 15 min. to an aqueous solution of acetoacetic acid[14] (prepared from 0.15 mole of ethyl acetoacetate). The mixture was neutralized (to congo red) by addition of sodium acetate and heated to 75°. After cooling the solution, the solid that formed was collected and recrystallized from Skellysolve C,[15] giving 6.5 g. (18%, based on 4-chloro-2-nitrobenzaldehyde) of pyruvaldehyde 1-(5-chloro-2-formylphenylhydrazone) as pale yellow needles, m.p. 140–141°. Although the following analysis indicates the product to be of the usual analytical purity expected in preparative work, the infrared spectrum of the analytical sample contained weak bands and shoulders indicative of minute traces of 3-acetyl-7-chlorocinnoline.

Anal. Calcd. for $C_{10}H_9N_2O_2Cl$: C, 53.47; H, 4.04; N, 12.46; Cl, 15.78. Found: C, 54.04; H, 4.09; N, 12.44; Cl, 15.92.

3-Acetyl-7-chlorocinnoline (VIIb).—Pyruvaldehyde 1-(5-chloro-2-formylphenylhydrazone) (1.0 g., 0.0044 mole) was carefully dissolved in 50 ml. of cold, concentrated sulfuric acid. The resulting solution was allowed to stand overnight, poured onto crushed ice, and filtered. The filtrate was neutralized (to congo red) by addition of sodium acetate and refiltered. The combined solids were recrystallized from Skellysolve C,[15] giving 0.36 g. (39%) of 3-acetyl-7-chlorocinnoline as pale yellow needles, m.p. 211–212°.

(12) Melting points are corrected. Analyses by Micro-Tech Laboratories, Skokie, Ill.

(13) L. I. Smith and J. W. Opie in E. C. Horning, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 56.

(14) The resultant solution will be referred to hereafter as the aqueous solution of acetoacetic acid.

(15) A hydrocarbon solvent, b.p. 88–98°.

(16) D. S. Breslow, E. Baumgarten and C. H. Hauser, THIS JOURNAL, **66**, 1286 (1944).

(17) A hydrocarbon solvent, b.p. 64–69°.

Anal. Calcd. for $C_{10}H_7N_2OCl$: C, 58.13; H, 3.42; N, 13.55. Found: C, 58.38; H, 3.58; N, 13.55.

When the sulfuric acid was replaced by 50 ml. of 20% hydrochloric acid and the resultant mixture was stirred on the steam-bath for 4–24 hr. and worked up as described above, a mixture of the cyclized and uncyclized materials was obtained.

Ethyl Glyoxalate 5-Chloro-2-formylphenylhydrazone (VIIIb) and 3-Carbethoxy-7-chlorocinnoline (IXb).—A diazonium salt solution, prepared as in the preparation of pyruvaldehyde 1-(5-chloro-2-formylphenylhydrazone), was added over a period of 15 min. to an aqueous solution of 0.15 mole of ethyl hydrogen malonate (*vide supra*) cooled to 0° in an ice-bath. The mixture was neutralized (to congo red) by addition of sodium acetate and heated to 75°. After cooling the solution, the solid that formed was collected and recrystallized from Skellysolve C,[15] giving 2.3 g. (6%, based on 4-chloro-2-nitrobenzaldehyde) of ethyl glyoxalate 5-chloro-2-formylphenylhydrazone as pale yellow needles, m.p. 79–80°. The infrared spectrum of this material contained bands indicative of minute traces of 3-carbethoxy-7-chlorocinnoline.

Anal. Calcd. for $C_{11}H_{11}N_2O_3Cl$: C, 51.88; H, 4.35; N, 11.00; Cl, 13.92. Found: C, 52.21; H, 3.87; N, 11.51; Cl, 14.15.

Attempts to cyclize this material by treatment with dilute hydrochloric acid or with concentrated sulfuric acid as described above for 3-acetyl-7-chlorocinnoline were not successful. However, when the preparation of the ethyl glyoxate 5-chloro-2-formylphenylhydrazone was repeated with no intentional deviation from the above procedure, the product was a mixture (infrared spectrum) of cyclized and uncyclized material, 2.5 g., m.p. 75–150°. By repeated recrystallization from Skellysolve C[15] 0.4 g. of 3-carbethoxy-7-chlorocinnoline was obtained as long, pale yellow needles, m.p. 200–201°.

Anal. Calcd. for $C_{11}H_9N_2O_2Cl$: C, 55.82; H, 3.83; N, 11.81. Found: C, 55.70; H, 3.98; N, 12.11.

LINCOLN 8, NEBRASKA

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

Steroidal Sapogenins. XLVI. Side Chain Structure of 20-Isosapogenins[2,3]

BY MONROE E. WALL AND HENRY A. WALENS

RECEIVED NOVEMBER 7, 1957

Dehydration of 20-hydroxytigogenin acetate (I) gave the unsaturated olefin II. The structure of II was established by hydroxylation with osmium tetroxide followed by cleavage with periodic acid to give IV. Catalytic hydrogenation of II in neutral solvents gave 20-isotigogenin (VII).

The stereochemistry of the sapogenin spiroketal side chain has been a subject of considerable interest in recent years. As the result of contributions from a number of laboratories, the structure of the spiroketal side chain of naturally occurring sapogenins seems well established and it is now generally agreed that such compounds differ only at C_{24}.[4a,b]

A new class of sapogenins obtained by treatment of a pseudosapogenin with acetic acid or dilute hydrochloric acid was obtained recently almost simultaneously in several laboratories.[5a–e] The stereochemistry of the spiroketal side chain of this class of compounds, which we wish to call 20-isosapogenins, has not been settled. This paper reports a partial synthesis of 20-isotigogenin acetate and of 20α-hydroxy-20-isotigogenin acetate which establishes in unequivocal fashion the side-chain structure of 20-isosapogenins of the 25D-series.

Oxidation of 20-isotigogenin acetate[6] with chromium trioxide in acetic acid gave a mixture of 3β,16β-dihydroxy-allopregnane-20-one 3-acetate 16-γ-methylglutarate and a new hydroxylated sapogenin (I). Compound I was obtained in approximately 45% yield and was separated easily by crystallization or chromatography from the acidic side chain cleavage product. Formulation of I as a probable 20-hydroxysapogenin was based on the following evidence. The optical rotation and infrared spectrum of I indicated that the spiroketal system was intact. The analytical constants for carbon and hydrogen were in agreement for a sapogenin with one additional hydroxyl group, substantiated by the infrared spectrum which showed a strong band at 3510 cm.$^{-1}$. This hydroxyl was tertiary as indicated by the fact that it could not be further oxidized, nor acetylated with hot pyridine–acetic anhydride and was dehydrated easily under mild conditions. On this basis compound I was at this stage designated as 20-hydroxytigogenin acetate with unspecified stereochemistry at C_{20}.

Dehydration of I with thionyl chloride in pyridine gave a new unsaturated sapogenin, formulated as $\Delta^{20(21)}$-tigogenin acetate (II). The latter was the key intermediate in all our subsequent work. The carbon and hydrogen analysis of II was in accord with the loss of one mole of water in going from I to II. This was confirmed by the infrared spectrum which showed absence of hydroxyl bands and new bands at 3080, 1797, 1665 and 903 cm.$^{-1}$ indicative of unsaturation, probably of a $R_1R_2{=}CH_2$ type.[7] That the unsaturated grouping was indeed a $C^{20(21)}$-methylene was proved as follows. Reaction of II with osmium tetroxide in benzene gave the diol-monoacetate III which, on

(1) A laboratory of the Eastern Utilization Research and Development Division, Agricultural Research Service, United States Department of Agriculture. Article not copyrighted.

(2) Paper XLV, Wall and Serota, THIS JOURNAL, **79**, 6481 (1957).

(3) Presented at second Delaware Valley Regional ACS Meeting, Philadelphia, Pa., February 5, 1958, and at 133rd National ACS Meeting, San Francisco, Calif., April 13–18, 1958.

(4) (a) Pertinent literature through 1955 is cited in a paper by M. E. Wall, *Experientia*, **11**, 340 (1955); (b) R. K. Callow and P. N. Massy-Beresford, *Chemistry & Industry*, 1146 (1956).

(5) (a) M. E. Wall, C. R. Eddy and S. Serota, THIS JOURNAL, **76**, 2849 (1954); **77**, 1230 (1955); (b) J. B. Ziegler, W. E. Rosen and A. C. Shabica, *ibid.*, **76**, 3865 (1954); **77**, 1223 (1955); (c) R. K. Callow and V. H. T. James, *Chemistry & Industry*, 691 (1954); (d) D. H. W. Dickson, J. Elks, R. M. Evans, A. G. Long, J. F. Oughton and J. E. Page, *ibid.*, 692 (1954); (e) R. K. Callow, D. H. W. Dickson, J. Elks, R. M. Evans, V. H. T. James, A. G. Long, L. F. Oughton and J. E. Page, *J. Chem. Soc.*, 1966 (1955).

(6) M. E. Wall and H. A. Walens, THIS JOURNAL, **77**, 5661 (1955).

(7) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen & Co., Ltd., London, 1954, pp. 31–47.