Anal. Calcd for $C_{12}H_{16}N_3O_8PLi_2 \cdot 2H_2O$: C, 35.05; H, 4.90; N, 10.22; P, 7.53. Found: C, 35.11; H, 4.87; N, 10.15; P, 7.37.

5'-Chloroacetamido-5'-deoxythymidine 3'-Phosphate Disodium Salt (21).—5'-Amino-5'-deoxythymidine 3'-phosphate inner salt (**19**, 385 mg) and Na_2CO_3 (297 mg) were dissolved in a mixture of methanol (5 ml) and water (5 ml) and the solution was stirred at 0°. Chloroacetic anhydride (342 mg) was added. As the reaction progressed, the chloroacetic anhydride dissolved in the reaction media. After stirring at 0° for 20 min, tlc (cellulose sheets, pc system A) indicated that the reaction was complete (product R_f 0.47, starting material R_f 0.26). The solution was concentrated *in vacuo* to a small volume. Water was added and the solution was lyophilized to give 920 mg of crude **21**. Compound **21** was purified by ppc (18 sheets of 3 MM paper, pc system A) to afford 580 mg of homogeneous solid with a low ϵ value: uv max 267 mμ (ϵ 5600) as a dihydrate, uv min 234 mμ (ϵ 2300). The solid was extracted with three portions of 2-propanol (10 ml). The 2-propanol extracts were discarded. The residue (560 mg, ϵ 5800) was extracted with three portions of ethanol (10 ml). The ethanol extract had no significant uv absorption and was discarded. The residue (300 mg, ϵ 8100) was purified for analysis by fractional precipitation from water–ethanol mixtures. Five fractions were collected. All five fractions were contaminated with a slower migrating impurity by tlc (cellulose tlc sheets, pc system A). The supernatants from the five fractions were combined and concentrated *in vacuo*. The residue (100 mg, ϵ 9200) was homogeneous by tlc. The solid was fractionally precipitated from water–2-propanol mixtures. Two fractions were collected. Fraction 2 (55 mg) was dissolved in water (10 ml) and the solution was concentrated *in vacuo* (repeated four times). The residue was dissolved in water again and the solution was lyophilized to give 50 mg of pure **21**: uv max 267 mμ (ϵ 9700), uv min 234 mμ (ϵ 2500), 250/260 (0.66), 260/270 (0.97), 270/280 (1.53).

Anal. Calcd for $C_{12}H_{15}ClN_3O_8PNa_2 \cdot 2H_2O$: C, 30.17; H, 4.00; N, 8.79; P, 6.48; Cl, 7.42. Found: C, 30.18; H, 3.83; N, 8.44; P, 6.45; Cl, 6.78.

5'-*N*-(*O*-Ethylcarbamoyl)-5'-deoxythymidine 3'-Phosphate Disodium Salt (22).—5'-Amino-5'-deoxythymidine 3'-phosphate inner salt (**19**, 300 mg) and Na_2CO_3 (310 mg) were dissolved in a mixture of methanol (4 ml) and water (4 ml) and the solution was stirred at 0°. Ethyl chloroformate (135 mg) was added dropwise over a period of 5 min. The reaction mixture was stirred for an additional 10 min at 0°. The course of the reaction was monitored by tlc (cellulose tlc sheets, pc system A) and showed one spot (R_f 0.70), different from starting material (R_f 0.47). The reaction mixture was neutralized with 0.3 *N* HCl solution and concentrated *in vacuo* to a small volume. Water was added and the solution was lyophilized to give 500 mg of crude **22**. The product was purified by ppc (pc system A, 12 sheets of 3 MM paper) to afford 250 mg of homogeneous **22**. Compound **22** was purified further by fractional precipitation from water–2-propanol mixtures. Five fractions were collected. Fraction 2 was dissolved in water (10 ml) and the solution was concentrated *in vacuo* (repeated three times). The residue was dissolved in water again and lyophilized to give 40 mg of pure **22**: uv max 267 mμ (ϵ 9700), uv min 234 mμ (ϵ 2500), 250/260 (0.67/270 (0.98), 270/280 (1.62).

Anal. Calcd for $C_{13}H_{18}N_3O_9PNa_2 \cdot 2H_2O$: C, 32.98; H, 4.69; N, 8.88; P, 6.55. Found: C, 33.27; H, 4.91; N, 9.04; P, 6.33.

Registry No.—**2**, 42214-24-4; **3**, 25442-42-6; **4**, 29706-84-1; **5**, 30516-87-1; **6**, 15981-92-7; **8**, 30516-88-2; **9**, 29706-87-4; **10**, 29706-88-5; **11**, 42214-32-4; **12**, 42214-33-5; **13**, 42214-34-6; **14**, 42214-35-7; **15**, 19316-85-9; **16**, 29912-68-3; **17**, 42214-38-0; **18**, 29706-89-6; **19**, 42319-49-3; **20**, 42214-40-4; **21**, 42214-41-5; **22**, 42214-42-6.

General Methods of Synthesis of Indole Alkaloids. XII. Syntheses of *dl*-18,19-Dihydroantirhine and Methyl Demethylilludinate[1,2]

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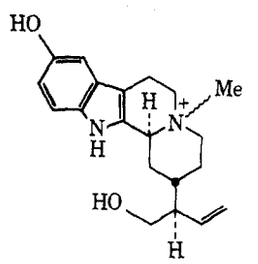
Received July 16, 1973

Methyl 4-carbomethoxymethylnicotinate was prepared from 4-methylnicotinic acid and condensed with acetaldehyde and with 3,3-dimethylcyclopentanone. Esterification, reduction, and oxidation of the first condensation product led to 4-(1-hydroxy-2-butyl)nicotinic lactone and thence in three steps to a derivative of antirhine, while esterification and cyclization of the second condensation product afforded an illudinine derivative.

The two-reaction sequence of partial hydrogenation of 1-alkyl-3-acylpyridinium salts and cyclization of the resultant 2-piperideines has constituted the backbone of alkaloid synthesis of a large variety of structure types.[3] This scheme of synthesis now has been exploited for the construction of a base structurally representative of the hunterburnine α- and β-metho salts (**1**),[4] vallesiachotamine (**2**),[5] and antirhine (**3**),[6] while intermediates on route to this base have been utilized for the synthesis of a derivative of illudinine (**4**).[7]



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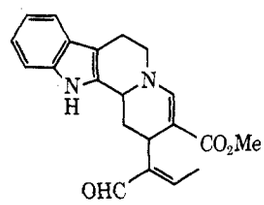

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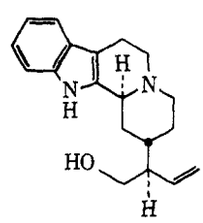

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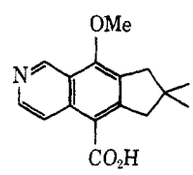


4

(1) Dedicated to Professor Edgar Lederer on the occasion of his 65th birthday.

(2) (a) This investigation was supported by the U. S. Public Health Service. (b) Part XI: E. Wenkert and G. D. Reynolds, *Syn. Commun.*, **3**, 241 (1973).

(3) E. Wenkert, *Accounts Chem. Res.*, **1**, 78 (1968).

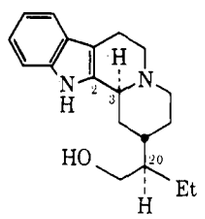
(4) J. D. M. Asher, J. M. Robertson, G. A. Sim, M. F. Bartlett, R. Sklar, and W. I. Taylor, *Proc. Chem. Soc., London*, 72 (1962); C. C. Scott, G. A. Sim, and J. M. Robertson, *ibid.*, 355 (1962); M. F. Bartlett, B. Korzun, R. Sklar, A. F. Smith, and W. I. Taylor, *J. Org. Chem.*, **28**, 1445 (1963); J. D. M. Asher, J. M. Robertson, and G. A. Sim, *J. Chem. Soc.*, 6355 (1965).

(5) C. Djerassi, H. J. Monteiro, A. Walser, and L. J. Durham, *J. Amer. Chem. Soc.*, **88**, 1972 (1966).

(6) S. R. Johns and J. A. Lamberton, *Chem. Commun.*, 229 (1967); S. R. Johns, J. A. Lamberton, and J. L. Occolowitz, *Aust. J. Chem.*, **20**, 1463 (1967); *cf.* also Y. K. Sawa and H. Matsumura, *Tetrahedron*, **25**, 5319 (1969).

(7) M. S. R. Nair, H. Takeshita, T. C. McMorris, and M. Anchel, *J. Org. Chem.*, **34**, 240 (1969).

18,19-Dihydroantirhine (5).—Under the challenge of three chiral centers in its structure, the total, stereospecific synthesis of dihydroantirhine (**5**) *via* the route first perfected for the synthesis of corynanthediol[8] was undertaken. While the proper 3,15-trans relationship was expected to arise in the cyclization step creating the C(2)–C(3) bond,[8] special attention had to be paid to the stereochemistry of C(20) on the rotationally unrestricted hydroxybutyl side chain. Hence, a scheme of synthesis was designed to maintain full stereochemical control by incorporation of part of the side chain into a ring system and introduction of the proper C(20) configuration onto the thus restrained side chain. Lactone **6** became the first important synthesis goal.



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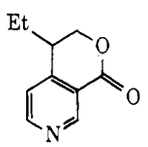
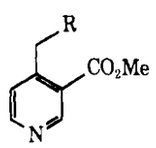
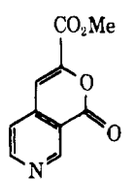


6

Base-catalyzed condensation of methyl oxalate with methyl 4-methylnicotinate (**7a**)[9] yielded the enolate salt of the keto diester **7b**, whose neutralization gave lactone **8**. Alkaline hydrolysis of the salt, decar-

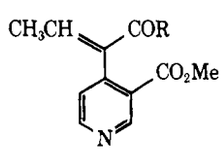


7a, R = H
b, R = $COCO_2Me$
c, R = CO_2Me

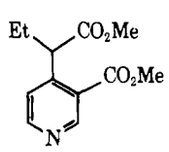


8

boxylation of the resultant keto diacid by oxidation with alkaline hydrogen peroxide, and esterification with methanolic acid led to methyl 4-carbomethoxymethylnicotinate (**7c**). Base-induced condensation of the latter with acetaldehyde and reesterification of the product[10] afforded diester **9a**,[12] whose hydrogenation produced the nicotinic ester derivative **10**.



9a, R = OMe
b, R = CO_2Me

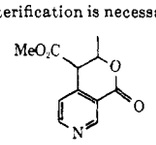


10

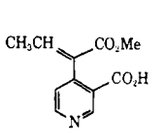
(8) E. Wenkert, K. G. Dave, and F. Haglid, *J. Amer. Chem. Soc.*, **87**, 5461 (1965).

(9) J. L. Webb and A. H. Corwin, *J. Amer. Chem. Soc.*, **66**, 1456 (1944).

(10) In analogy with the Stobbe condensation,[11] a lactone (i) is the initial intermediate and the β-elimination product ii its successor. Hence, a subsequent esterification is necessary.



i



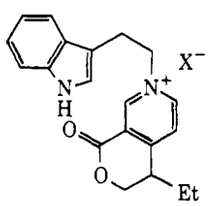
ii

(11) W. S. Johnson and G. H. Daub, "Organic Reactions," Vol. VI, Wiley, New York, N. Y., p 1.

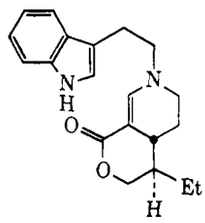
(12) Similar condensation of **7b** with acetaldehyde yielded **9b** (see Experimental Section).

Lithium aluminum hydride reduction thereof and oxidation of the diol product with manganese dioxide yielded the desired lactone **6**.

Alkylation of lactone **6** with tryptophyl bromide gave a pyridinium salt (**11a**) whose hydrogenation[3] led to a tetrahydropyridine. The latter was assigned stereostructure **12** on the assumption of the hydro-



11a, X = Br
b, X = ClO_4

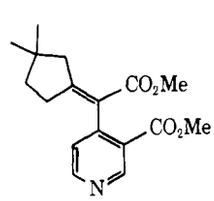


12

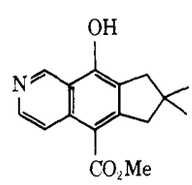
genation occurring under thermodynamic control in the absence of overriding steric factors and the 15,20-trans stereochemistry being the energetically more favorable one. Alkaline hydrolysis (followed by decarboxylation and cyclization[8]) of **12** afforded *dl*-18,19-dihydroantirhine (**5**) spectrally identical with a sample derived from the natural product.[13,14]

Methyl Demethylilludininate (14).—In view of the availability of diester **7c** and the favorable experience of its condensation with a carbonyl compound (**7c** → **9a**), it was decided to synthesize the illudinine (**4**) ring system from **7c** by a related reaction sequence.

Base-catalyzed condensation of methyl 4-carbomethoxymethylnicotinate (**7c**) with 3,3-dimethylcyclopentanone,[15] followed by esterification of the resultant acid esters (*cf.* ref 10), yielded a mixture of diester **13** and its stereoisomer. Their further base treatment under equilibrium conditions was expected to induce the aromatic ester moiety to condense into the less sterically encumbered allylic site of the cyclopentane unit. On exposure of the diester mixture to potassium *tert*-butoxide in *tert*-butyl alcohol, a single product was obtained whose spectral properties revealed it to be the illudinine derivative **14**.



13



14

Experimental Section

Melting points were determined on a Reichert micro hot stage and are uncorrected. Proton magnetic resonance spectra of solutions with tetramethylsilane acting as internal standard were recorded on Varian Associates A-60 and HA-100 spectrometers.

Methyl 4-Carbomethoxymethylnicotinate (7c).—Freshly cut potassium, 5 g, was dissolved in 60 ml of *dry tert*-butyl alcohol (refluxed and distilled over calcium hydride) under dry nitrogen. Dry, peroxide-free 1,2-dimethoxyethane (refluxed, distilled, and

(13) The authors are indebted to Dr. S. Johns for a gift of a sample of *l*-antirhine.

(14) For other syntheses of dihydroantirhine, see T. Kimara and Y. Ban, *Chem. Pharm. Bull.*, **17**, 296 (1969); H.-P. Husson, L. Chevolot, Y. Langlois, C. Thal, and P. Potier, *Chem. Commun.*, 930 (1972).

(15) T. Henshall, *J. Soc. Chem. Ind., London*, **62**, 127 (1943); H. Pines, F. J. Pavlik, and V. N. Ipatieff, *J. Amer. Chem. Soc.*, **73**, 5738 (1951).

stored over sodium wire), 200 ml, was added and the mixture was cooled to 10°. Methyl 4-methylnicotinate (**7a**),[9] 12.8 g, was added and the mixture was stirred for 5 min. Thereupon 12.8 g of dimethyl oxalate was added in one portion and the mixture was stirred under dry nitrogen for 18 hr. The resultant solid paste was poured into 600 ml of dry ether and the flocculent, yellow precipitate was filtered onto a sintered glass funnel under a stream of dry nitrogen and washed with 50 ml of dry ether. The dry enolate salt was dissolved in 100 ml of water. After a few minutes lactone **8** began to precipitate, whereupon a solution of 13 g of potassium hydroxide in 65 ml of water was added and the orange-red solution was stirred at room temperature for 2 hr. (Absence of lactone precipitation generally reflected failure of the initial condensation.) Next, eight 2.4-ml portions of 30% hydrogen peroxide were added to the stirring solution at 0–5° in a cold room over a period of 24 hr. (Both peroxide concentration and temperature were critical for maintaining a reasonable yield of final product.) The mixture was stirred at 0–5° for another 12 hr, whereupon water was removed from the light yellow solution by freeze-drying up to 50° (preferably below room temperature). Further drying at 0.2–0.5 Torr for 12 hr left a yellow-green solid. (Insufficient drying led to failure of the subsequent esterification.) The latter was stirred in 500 ml of dry methanol at −70° for 2 hr. Methanol, 200 ml, saturated with hydrogen chloride gas and precooled to −70° was added and the mixture was stirred and allowed to come to room temperature. (Neutralization of the dicarboxylate salt and passage through the isoelectric point at temperatures above −70° resulted in extensive decarboxylation.) It then was stirred, protected by a drying tube, at room temperature for 4 days. The pale orange mixture was poured slowly onto 800 ml of a methylene chloride suspension of an excess of sodium bicarbonate, the inorganic material was filtered, and the filtrate was dried over anhydrous sodium carbonate. Evaporation of the filtrate under vacuum at 35° yielded a viscous, orange oil whose pmr spectrum revealed it to contain *ca.* 5% of starting ester (**7a**). Chromatography of the oil on alumina, activity IV, and elution with benzene gave 12.3 g of a low-melting solid. (Distillation thereof led to its total destruction.) Crystallization from hexane afforded colorless plates of diester **7c**: mp 51.5–52°; ir (KBr) C=O 5.73 (s), 5.82 (s), C=C 6.28 (m), 6.42 μ (m); pmr (CCl_4) δ 3.64 (s, 3, OMe of aliphatic ester), 3.87 (s, 3, OMe of aromatic ester), 3.98 (s, 2, methylene), 7.10 [d, 1, J = 5.0 Hz, C(5) H], 8.53 [d, 1, J = 5.0 Hz, C(6) H], 9.07 [s, 1, C(2) H].

Anal. Calcd for $C_{10}H_{11}O_4N$: C, 57.41; H, 5.30; N, 6.70: Found: C, 57.70; H, 5.36; N, 6.65.

Lactone 8.—A solution of 2.0 g of the enolate salt of **7b** in 10 ml of water was brought to pH 6 with 2 *M* hydrochloric acid and the resultant precipitate was filtered, dried, and sublimed at 150° (15 Torr). Crystallization of the sublimate from methanol gave 0.9 g of colorless prisms of lactone **8**: mp 187–188°; ir (KBr) C=O 5.70 (s), 5.81 (s), C=C 6.12 (m), 6.29 μ (s); uv (MeOH) λ_{max} 221 nm (ε 5100), 242 (3500), 250 (3200), 272 (2300), 291 (2400), 381 (1000); pmr ($CDCl_3$) δ 3.99 (s, 3, OMe), 7.45 (s, 1, enol methine), 7.48 (d, 1, J = 5.0 Hz, pyridine β′ H), 8.95 (d, 1, J = 5.0 Hz, pyridine α′ H), 9.52 (s, 1, pyridine α H).

Anal. Calcd for $C_{10}H_7O_4N$: C, 58.54; H, 3.44; N, 6.83. Found: C, 58.57; H, 3.61; N, 6.85.

Methyl 4-(α-Carbomethoxypropenyl)nicotinate (9a).—Diester **7c**, 2.90 g, was added to a solution of potassium *tert*-butoxide, prepared from 0.63 g of freshly cut potassium in 5 ml of *tert*-butyl alcohol, in 200 ml of dry 1,2-dimethoxyethane and the mixture was stirred under nitrogen at room temperature for 10 min. It then was cooled to 0° and a solution of 3 ml of freshly distilled acetaldehyde in 100 ml of dry 1,2-dimethoxyethane was added dropwise over a period of 45 min. The mixture was stirred under nitrogen for 18 hr and then evaporated. The residue was dissolved in 200 ml of methanol saturated with hydrogen chloride gas and the mixture was left at room temperature for 4 days. It then was poured onto a methylene chloride suspension of an excess of sodium bicarbonate and filtered. The filtrate was dried over anhydrous sodium carbonate and evaporated. Chromatography of the residue on alumina, activity IV, and elution with cyclohexane gave a pale yellow oil whose distillation [150° (0.05 Torr)] yielded 1.80 g of colorless liquid diester **9a**: ir (neat) C=O 5.81 (s), C=C 6.11 (w), 6.31 (m), 6.50 μ (m); pmr (CCl_4) δ 1.68 [d, 3, J = 7.0 Hz, Me of major (88%) isomer], 2.25 [d, 3, J = 7.0 Hz, Me of minor (12%) isomer], 3.62, 3.82 (s, 3 each, methoxyls), 7.05 [d, 1, J = 5.0 Hz, C(5) H], 7.07 (q, 1, J = 7.0 Hz, olefinic H), 8.65 [d, 1, J = 5.0 Hz, C(6) H], 9.10 [s, 1, C(2) H]. (The liquid turned yellow and its purity decreased on storage.)

Anal. Calcd for $C_{12}H_{13}O_4N$: N, 5.95. Found: N, 5.86.

Keto Diester 9b.—A solution of 1.0 g of methyl 4-methylnicotinate (**7a**) and 0.90 g of potassium *tert*-butoxide in 30 ml of 1:1 *tert*-butyl alcohol and 1,2-dimethoxyethane was kept under nitrogen at 0° for 10 min. Dimethyl oxalate, 1.0 g, was added and the mixture was stirred at room temperature for 5 hr. It was cooled to 0° and a solution of 1.0 g of acetaldehyde in 10 ml of 1,2-dimethoxyethane was added dropwise over a period of 30 min. The mixture was stirred at room temperature for 18 hr and then evaporated under reduced pressure. The residue was dissolved in 50 ml of dry methanol, saturated with hydrogen chloride gas, and the solution was kept for 3 days. It then was neutralized with sodium bicarbonate and filtered. The filtrate was evaporated, the residue was extracted with chloroform, and the extract was washed with water, dried, and evaporated under vacuum. The residual, viscous, yellow oil, 1.5 g, solidified slowly. Crystallization from chloroform afforded 0.90 g of colorless needles of ester **7b**: mp 159–160°; ir (KBr) C=O 5.69 (s), 5.80 (s), C=C 6.24 μ (m); pmr (deuterioacetone) δ 1.38 (d, 3, J = 7.0 Hz, Me), 3.90, 4.28 (s, 3 each, methoxyls), 5.61 (q, 1, J = 7.0 Hz, olefinic H), 7.54 [d, 1, J = 5.0 Hz, C(5) H], 8.80 [d, 1, J = 5.0 Hz, C(6) H], 9.02 [s, 1, C(2) H].

Anal. Calcd for $C_{13}H_{13}O_5N$: N, 5.32. Found: N, 5.54.

Methyl 4-(α-Carbomethoxypropyl)nicotinate (10).—A mixture of 2.0 g of **9a** and 40 mg of platinum oxide in 80 ml of dry methanol was hydrogenated at atmospheric pressure and room temperature. After 24 hr, the mixture was filtered, the filtrate was evaporated, and the residual oil was chromatographed on alumina, activity IV. Elution with benzene yielded 1.7 g of colorless, liquid diester **10**: ir (neat) C=O 5.80 (s), C=C 6.30 (m), 6.46 μ (w); pmr (CCl_4) δ 0.91 (t, 3, J = 7.0 Hz, Me), 1.0–2.2 (m, 2, methylene), 3.61, 3.88 (s, 3 each, methoxyls), 4.58 (t, 1, J = 7.0 Hz, methine), 7.25 [d, 1, J = 5.0 Hz, C(5) H], 8.49 [d, 1, J = 5.0 Hz, C(6) H], 9.00 [s, 1, C(2) H].

Anal. Calcd for $C_{12}H_{15}O_4N$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.68; H, 6.63; N, 5.97.

Lactone 6.—A solution of 2.00 g of the diester **10** in 50 ml of ether was added dropwise to a suspension of 1.00 g of lithium aluminum hydride in 150 ml of ether over a period of 15 min and the mixture then was refluxed for 18 hr. Moist sodium sulfate was added and the suspension was shaken for 30 min. It then was filtered and the precipitate was washed with hot ethyl acetate. The combined filtrate and washings were dried over magnesium sulfate and evaporated. A mixture of the residual, colorless, viscous, liquid diol, 1.40 g, and 10.0 g of activated manganese dioxide[16] in 350 ml of dry ether was stirred at room temperature for 46 hr. It was filtered through Celite and the solid was washed with hot ethyl acetate. The combined filtrate and washings were dried and evaporated. Chromatography of the residual yellow oil on alumina, activity IV, and elution with benzene yielded 950 mg of colorless, liquid lactone **6**: ir (neat) C=O 5.79 (s), C=C 6.24 μ (s); pmr (CCl_4) δ 1.01 (t, 3, J = 7.0 Hz, Me), 1.2–2.0 (m, 2, methylene), 2.82 (m, 1, methine), 4.2–4.7 (m, 2, oxymethylene), 7.25 [d, 1, J = 5.0 Hz, C(5) H], 8.59 [d, 1, J = 5 Hz, C(6) H], 8.95 [s, 1, C(2) H]; yellow plates of its picrate, crystallized from methanol, had mp 153–154°.

Anal. Calcd for $C_{16}H_{14}O_9N_4$: C, 47.30; H, 3.47; N, 13.79. Found: C, 47.43; H, 3.73; N, 13.63.

Pyridinium Salt 11b.—A solution of 80 mg of lactone **6** and 101 mg of tryptophyl bromide in 30 ml of ether was stirred at room temperature under nitrogen for 36 hr. The mixture was evaporated and the residue was washed with dry ether. Since the resultant salt could not be induced to crystallize, it was treated with a saturated, aqueous solution of sodium perchlorate. Crystallization of the new salt from methanol yielded 100 mg of **11b**: mp 150–153°; ir (KBr) NH 2.90 (s), 2.98 (s), 3.13 (s), C=O 5.90 (s), C=C 6.15 μ (m).

Anal. Calcd for $C_{20}H_{21}O_6N_2Cl$: C, 55.60; H, 4.87; N, 6.50. Found: C, 55.84; H, 5.14; N, 6.65.

***dl*-18,19-Dihydroantirhine (5).**—A mixture of 20 mg of 10% palladium on charcoal and 1.2 ml of triethylamine in 15 ml of methanol was saturated with hydrogen and a solution of 100 mg of salt **11b** in 15 ml of methanol was then added. The mixture was hydrogenated at atmospheric pressure. After an uptake of 2 equiv of hydrogen, it was filtered and the filtrate was evaporated.

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Chromatography of the residue on alumina, activity IV, and elution with benzene gave 40 mg of oily **12**: ir (CCl_4) NH 3.18 (m), C=O 6.00 (s), C=C 6.32 μ (s). In view of its instability, it was used for the next reaction without further purification.

A solution of 40 mg of **12** in 10 ml of 10% methanolic potassium hydroxide was stirred at room temperature under nitrogen for 30 hr. It was neutralized with 10% hydrochloric acid and evaporated. Extraction of the residue with ethanol and evaporation of the extract gave 10 mg of a viscous oil which crystallized slowly. Crystallization from ethyl acetate–ethanol yielded 4 mg of prisms of *dl*-18,19-dihydroantirhine (**5**): mp 95–97.5°; infrared, ultraviolet, mass spectral, and tlc characteristics identical with those of an authentic sample;[6,13] *m/e* 298.204516 (calcd 298.204503).

Methyl Demethylilludinate (14).—A solution of dry potassium *tert*-butoxide (from 620 mg of potassium) and 3.24 g of diester **7c** in 25 ml of 1,2-dimethoxyethane was added dropwise to 1.75 g of 3,3-dimethylcyclopentanone[15] over a 1-hr period and the mixture was stirred at room temperature under nitrogen for 15 hr. Hydrochloric acid (50 ml of 3 *N*) was added and the mixture was evaporated at 50° to dryness. The residue was dried further in a vacuum desiccator for 12 hr and then dissolved in 50 ml of methanol saturated with hydrogen chloride gas. After 2 hr, the mixture was worked up in a previously described manner[17] and the crude product was chromatographed on alumina (activity III) and eluted with a 3:2 mixture of cyclohexane–benzene. Crystallization of the product from pentane gave 2.98 g of colorless crystals, mp 38–45°, whose sublimation afforded the diesters **13** and its stereoisomer: mp 45–55°; ir (KBr) C=O 5.78 (s), 5.81 (s), C=C 6.12 (m), 6.31 (m), 6.48 (m); uv (MeOH) λ_{max} 224 nm (log ϵ 4.36); pmr ($CDCl_3$) δ 0.93 (s, 3, Me), 1.08 (s, 3, Me), 1.62 (t, 2, J = 8 Hz, CH_2 of major isomer), 1.88 (broad s, 2,allyl CH_2 of major isomer), 2.18 (t, 2, J = 8 Hz, CH_2 of minor isomer), 2.83 (broad s, 2, allyl CH_2 of minor isomer), 3.10 (t, 2, J = 8 Hz, allyl CH_2 of major isomer), 3.61 (s, 3, OMe), 3.82 (s, 3, OMe), 7.12 [t, 1, J = 4 Hz, C(5) H], 8.68 [d, 1, J = 4 Hz, C(6) H], 9.13 [broad s, 1, C(2) H].

Anal. Calcd for $C_{17}H_{21}O_4N$: C, 67.29; H, 6.98; N, 4.62. Found: C, 67.13; H, 7.08; N, 4.63.

A solution of 733 mg of diester **13** and its stereoisomer in 5 ml of dry 1,2-dimethoxyethane was added to a solution of potassium *tert*-butoxide (from 104 mg of potassium) in 25 ml of 1,2-dimethoxyethane and the intensely red solution was stirred under nitrogen for 0.5 hr. The color had disappeared and the mixture was evaporated to dryness. The residue was treated with 10 ml of water and the mixture was brought to pH 6 with 5% hydrochloric acid and extracted with methylene chloride. The extract was dried over anhydrous sodium sulfate and evaporated. Crystallization of the residue from ethyl acetate yielded 525 mg of yellow, crystalline ester **14**: mp 220° dec; ir (Nujol) C=O 5.87 (s), C=C 6.14 (s), 6.27 (w), 6.38 (s); uv (MeOH) λ_{max} 242 nm (log 4.63), 285 (4.03), 307 (4.01), 333 (3.98), 385 (3.66); $\lambda_{shoulder}$ 260 nm (log ϵ 4.33), 348 (3.93); pmr (DMSO-d_6) δ 2.85 (s, 2, CH_2), 3.08 (s, 2, CH_2), 3.92 (s, 3, OMe), 8.23 (d, 1, J = 6 Hz, pyridine β H), 8.45 (d, 1, J = 6 Hz, pyridine α H), 9.50 (s, 1, pyridine α' H).

Anal. Calcd for $C_{16}H_{17}O_3N$: C, 70.83; H, 6.32; N, 5.16. Found: C, 71.10; H, 6.47; N, 5.33.

Registry No.—**5**, 42289-79-2; **6**, 42253-62-3; **6** picrate, 42289-80-5; **7a**, 33402-75-4; **7b** enolate, 42253-64-5; **7c**, 33402-74-3; **8**, 33402-73-2; **9a**, 42253-67-8; **9b**, 42253-68-9; **10**, 42253-69-0; **11b**, 42253-70-3; **12**, 42253-71-4; **13**, 42253-72-5; **13** stereoisomer, 42253-73-6; **14**, 42253-74-7; dimethyl oxalate, 553-90-2.

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Steroids Derived from Bile Acids. A Novel Side-Chain Degradation Scheme

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A four-step degradative sequence of methyl cholanate (**1**) and methyl lithocholate (**13**) is described with a 35 and 27% overall yield, respectively. The method involves conversion of the esters to the rearranged phenyl ketones (**4** and **16**) which are in turn subjected to a Norrish type II photoelimination. Ozonolysis of the final products leads to physiologically important steroid compounds.

In a recent publication[1] we have described a novel method for the degradation of the carbon chain of organic acids and their derivatives. The key substance in the sequence we have described is a phenyl ketone which is easily obtainable by an established[2] rearrangement procedure. In view of the intensive recent interest[3-7] in the photolysis of such compounds by Norrish type II processes, we have decided to utilize this reaction, combine it with a part of our previous scheme, and apply it to the degradation of the side chain of steroidal substrates. Thus a convenient modification of the original degradative sequence has resulted, the individual steps of which are outlined in Scheme I.

Results and Discussion

Samples of esters **1** and **13** were converted to the corresponding tertiary alcohols **2** and **14** by means of a standard Grignard reaction with phenylmagnesium bromide in nearly quantitative yields. Dehydration of the alcohols in acetic anhydride afforded the corresponding olefins **3** and **15**. The yields for this step were 85%. The olefins **3** and **15** were easily and quantitatively converted to the corresponding ketones **4** and **16** by means of the Kakis reaction.[2] This reaction in the present system generates a pair of diastereomers, epimeric around the C_{23} asymmetric carbon. Although not directly related to the degradative scheme, which utilizes the mixture, we thought it would be of theoretical as well as practical interest to separate the stereoisomers and to obtain the spectra and their physical constants. This seemed to be particularly appropriate since these compounds have never been prepared before and their physiological properties are not known. Separation was achieved by laborious thin-layer chromatography. The pure isomers were isolated and their melting points, optical rotations, and nmr spectra were obtained.

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