of 2.22 g (13.4 mmoles) of potassium iodide in 5 ml of water and the mixture was stirred and allowed to warm up to +5° over 15 min.

The mixture was diluted with water and extracted with methylene chloride. The extract was washed with water, dilute sodium thiosulfate solution, and finally with water, then dried, and evaporated to a dark oil which was chromatographed on 150 g of silica gel. The product (648 mg, 23%) was obtained after elution of the column with 3% ethyl acetate–petroleum ether followed by 5% ethyl acetate–petroleum ether. Crystallization from hexane gave 610 mg (22%) of off-white product, mp 212–215°. A final crystallization from *n*-hexane gave colorless crystals: mp 213–215°; λ_{max} 211 mμ (ε 34,800), 230 (sh) (11,000), and 284–293 (2050); $[\alpha]_D$ +252°; ν_{max}^{KBr} 857, 830, and 760 cm^{-1}; nmr 7.29 (d, C-2 H), 6.62 (d, C-4 H), 3.73 (s, OCH_3), and 0.95 (s, C-18 CH_3) ppm.

Anal. Calcd for $C_{19}H_{23}IO_2$ (410.29): C, 55.62; H, 5.65; I, 30.94. Found: C, 55.25; H, 5.90; I, 30.63.

Further elution of the column with 5% acetone–petroleum ether followed by 10% acetone–petroleum ether gave 1.39 g of material which was shown by tlc to consist of 1-acetoxy-3-methoxyestra-1,3,5(10)-trien-17-one (**9**) and 1-hydroxy-3-methoxyestra-1,3,5(10)-trien-17-one (**3**) in yields of 15 and 38%, respectively.

Registry No.—**3**, 13871-38-0; **5**, 6654-48-4; **6**, 6654-47-3; **7**, 14795-95-0; **8**, 13639-96-8; **9**, 14795-97-2; **10**, 14795-98-3; **11**, 14795-99-4; **12**, 14796-00-0; **13**, 14796-01-1.

1,11-Iminoestrones.[1] II. Some Derivatives and Reactions

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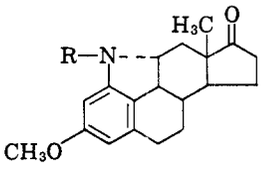
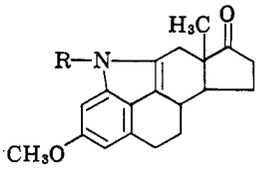
Received June 26, 1967

In part I[1] of this work, the synthesis and proof of structure of 1,11α-imino-3-methoxyestra-1,3,5(10)-trien-17-one (**1a**) and 1,11-imino-3-methoxyestra-1,3,5(10),9(11)-tetraen-17-one (**2a**) were outlined. The preparation of some N-substituted derivatives and several oxidative reactions of these compounds are now described.



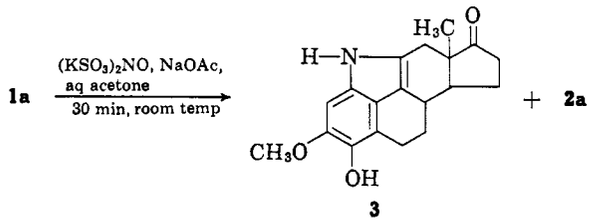


1a, R = H
b, R = H (HCl salt)
c, R = CH_3CO
d, R = *p*-ClC_6H_4CO
e, R = CH_3

2a, R = H
b, R = *p*-ClC_6H_4CO
c, R = CH_3

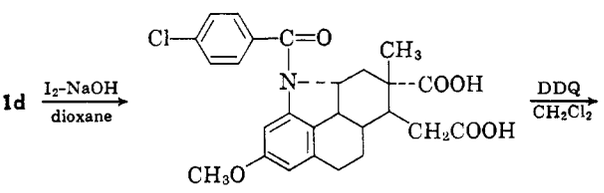
Iminoestrone **1a** was converted to its hydrochloride (**1b**), N-acetyl (**1c**), and N-*p*-chlorobenzoyl (**1d**) derivatives by conventional methods. An attempt to prepare the N-methyl derivative (**1e**) by refluxing **1a** with methyl iodide–potassium carbonate in methanol gave a very polar, water-soluble product which was, presumably, the methiodide of **1e**. The N-methyl derivative was successfully prepared, in 46% yield, by the reaction of **1a** with sodium hydride–methyl iodide in dimethylformamide–benzene solution at 35–40°. Dehydrogenation of the product (**1e**) with 10% palladium on carbon in refluxing xylene gave **2c** in a yield of 91%. While catalytic dehydrogenation of the N-*p*-chlorobenzoyl derivative (**1d**) was unsuccessful, this compound was smoothly dehydrogenated with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ)[2] in methylene chloride at room temperature to give the corresponding 9,11-dehydro derivative (**2b**) in 96% yield.

Teuber and Staiger[3] have shown that the oxidation of indolines with potassium nitrosodisulfonate (Fremy's salt) gives indoles and 5-hydroxyindoles and, with excess reagent, indoloquinones. Similarly, the reaction of **1a** with 2 moles of Fremy's salt gave hydroxyindole **3** in a yield of 54% plus a small yield of indole **2a**.

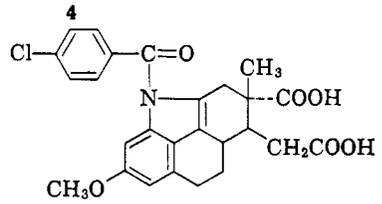


3

Oxidative cleavage of ring D of the *p*-chlorobenzoyl derivative, **1d**, with iodine–sodium hydroxide gave the 16,17-seco diacid **4** in 42% yield. Essentially the method of Heer and Miescher[4] was used except that methanol was replaced by dioxane to avoid ester formation.



4



5

Subsequent dehydrogenation of **4** with DDQ in methylene chloride at room temperature gave, in 77% yield, the desired 1,11-(*p*-chlorobenzoyl)imino-3-methoxy-16,17-secoestra-1,3,5(10),9(11)-tetraene-16,17-dioic acid (**5**), which has certain formal resemblances to the antiinflammatory drug, indomethacin.[5]

In the dehydrogenation of seco diacid **4** there was isolated a by-product (**6a**) in a yield of approximately 5%. This compound was shown to arise by further reaction of the product (**5**) with DDQ. Thus, the treatment of **5** with 2 equiv of DDQ in methylene

(1) For part I, see E. W. Cantrall, R. B. Conrow, and S. Bernstein, *J. Org. Chem.*, **32**, 3445 (1967).

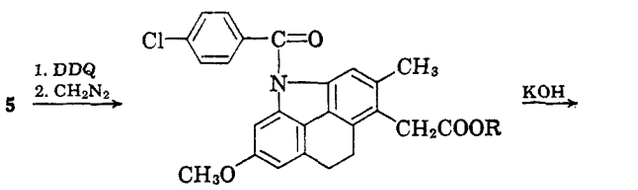
(2) For a recent review on dehydrogenations with DDQ, see D. Walker and J. D. Hiebert, *Chem. Rev.*, **67**, 153 (1967).

(3) H. J. Teuber and G. Staiger, *Ber.*, **87**, 1251 (1954); **89**, 489 (1956).

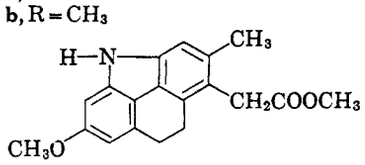
(4) J. Heer and K. Miescher, *Helv. Chim. Acta*, **28**, 156 (1945).

(5) T. Y. Shen, T. B. Windholz, A. Rosegay, B. E. Witzel, A. N. Wilson, J. D. Willett, W. J. Holtz, R. L. Ellis, A. R. Matzuk, S. Lucas, C. H. Stammer, F. W. Holly, L. H. Sarett, E. A. Risley, G. W. Nuss, and C. A. Winter, *J. Am. Chem. Soc.*, **85**, 488 (1963).

chloride at room temperature resulted in ring C decarboxylation–aromatization[6] to give, in 50% yield, the dihydrophenanthrene derivative **6a**. Reaction of **6a** with diazomethane gave the ester, **6b**, which, on hydrolysis of the labile *p*-chlorobenzoyl moiety, afforded compound **7**.

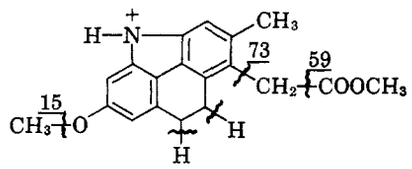


6a, R = H
b, R = CH_3



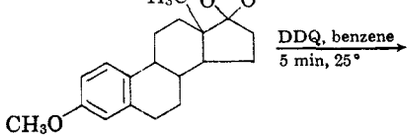
7

The structures of **6a**, **6b**, and **7** were established by spectral analysis (infrared, ultraviolet, nmr, and mass spectrometry). The nmr spectrum of **7** was particularly informative since all protons in the molecule can be accounted for and their chemical shifts are in agreement with those expected for the depicted structure (**7**). In the mass spectrum of **7**, the molecular ion (M^+) was the base peak and occurred at *m/e* 309 (calcd for $C_{19}H_{19}NO_3$, 309). The next most abundant peak occurred at *m/e* 250 which corresponds to the loss of a carbomethoxy function. Other significant peaks, in order of decreasing abundance, occurred at *m/e* 236, 248, and 235, arising from the fragmentations indicated.

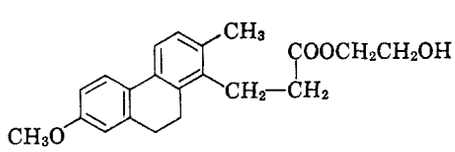


These results are consistent with the splitting pattern of related compounds.[7]

(6) A similar reaction involving ring C aromatization of estrone 3-methyl ether 17-ethylene ketal (i) with DDQ under mild conditions has been reported by S. G. Boots and W. S. Johnson, *J. Org. Chem.*, **31**, 1285 (1966).

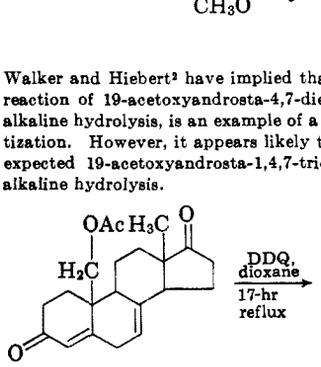


i

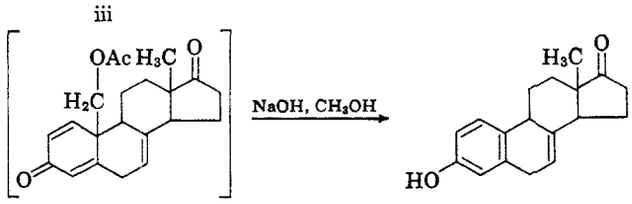


ii

Walker and Hiebert[2] have implied that the formation of equilin (v) by the reaction of 19-acetoxyandrosta-4,7-dien-3-one (iii) with DDQ, followed by alkaline hydrolysis, is an example of a direct, DDQ-mediated, ring A aromatization. However, it appears likely that this reaction may proceed *via* the expected 19-acetoxyandrosta-1,4,7-trien-3-one (iv) which then gives v on alkaline hydrolysis.



iii



iv v

The aromatization of compounds of type iv on mild alkaline hydrolysis has been reported by H. Hagiwara, *Yakugaku Zasshi*, **80**, 1671 (1960); *Chem. Abstr.*, **55**, 11463*i* (1961).

Experimental Section

Thin layer chromatography was carried out on glass plates coated with a 0.25-mm layer of silica gel G (Merck AG, Darmstadt) containing approximately 0.3% Radelin Phosphor GS-115 (U. S. Radium Corp.). Development was effected with benzene–acetone–water 2:1:2 (upper phase) unless otherwise noted. In preparative work a 0.5-mm layer on 20 × 20 cm plates was used. After development, the chromatograms were visualized by ultraviolet light and by spraying with a 10% phosphomolybdic acid–methanol solution. Solutions were dried over anhydrous sodium sulfate and all evaporations were under reduced pressure unless otherwise noted.

Magnesol, a hydrous magnesium silicate (Food Machinery Chemical Corp.), Celite, a diatomaceous silica (Johns-Manville), Florisil, a synthetic magnesium silicate adsorbent, 60–100 mesh (Floridin Corp.), silica gel (Davison Chemical Co.), 100–200 mesh, and Darco, activated carbon (Atlas Powder Co.) were used as received.

Melting points were determined on a Mel-Temp apparatus in open capillaries and are uncorrected. Infrared spectra were determined in pressed potassium bromide disks on a Perkin-Elmer Model 21 spectrophotometer. Ultraviolet spectra were determined in methanol solution on a Cary Model 11 recording spectrophotometer. Optical rotations were measured at 25° in chloroform solution, unless otherwise noted. Nuclear magnetic resonance spectra were determined on a Varian A-60 spectrometer with tetramethylsilane as internal standard in deuteriochloroform solution, unless otherwise noted. The chemical shifts are expressed in parts per million (ppm). Mass spectra were determined on an AEI MS-9 spectrometer (Associated Electrical Industries Ltd.). The infrared and nuclear magnetic resonance spectra and optical rotations were performed by W. Fulmor, G. O. Morton, and associates, the mass spectra by Dr. J. Karliner, and the elemental analyses by L. Brancone and associates.

1,11α-Imino-3-methoxyestra-1,3,5(10)-trien-17-one Hydrochloride (1b).—Anhydrous hydrogen chloride was passed over the surface of a stirred solution of 1.0 g (3.36 mmoles) of 1,11α-imino-3-methoxyestra-1,3,5(10)-trien-17-one (**1a**) in 150 ml of anhydrous ether plus 20 ml of methylene chloride. After the mixture became acidic, it was boiled to remove the methylene chloride and was then filtered. The collected product was washed with ether, refluxed with benzene, filtered off, and washed on the filter with acetone to remove any free amine. The yield was 880 mg (79%) of colorless amorphous solid: mp 250–270° dec; λ_{max} 230 (sh), 290 mμ (ε 8350, 3340); $[\alpha]D$ +95° (methanol); ν_{max}^{KBr} 2439 cm^{-1} (NH_2^+).

Anal. Calcd for $C_{19}H_{24}ClNO_2$ (333.84): C, 68.36; H, 7.24; N, 4.19; Cl, 10.62. Found: C, 68.33; H, 7.50; N, 4.25; Cl, 10.32.

1,11α-Acetylimino-3-methoxyestra-1,3,5(10)-trien-17-one (1c).—To a solution of 500 mg (1.68 mmoles) of the iminoestrone (**1a**) in 5 ml of acetic acid was added 1.0 ml of acetic anhydride and the solution warmed on the steam bath for 30 min. Water (5 ml) was added and heating continued for 15 min; then an additional 10 ml of water was added and the mixture extracted

(7) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure and Elucidation of Natural Products by Mass Spectrometry," Vol. I, Holden-Day, Inc., San Francisco, Calif., 1964, pp 42, 53–57.

with chloroform. The extract was washed with water until neutral, then dried, and evaporated to give 570 mg (100%) of a solid residue, mp 245–258°. A single crystallization from methylene chloride–ether gave 470 mg of colorless crystals: mp 250–256°; λ_{max} 220, 251, 299 mμ (ε 28,800, 10,850, 6780); $[\alpha]D$ +40°; ν_{max}^{KBr} 1656 (amide CO), 1631 cm^{-1} (aromatic).

Anal. Calcd for $C_{21}H_{25}NO_3$ (339.42): C, 74.31; H, 7.42; N, 4.13. Found: C, 73.93; H, 7.60; N, 4.32.

1,11α-(*p*-Chlorobenzoyl)imino-3-methoxyestra-1,3,5(10)-trien-17-one (1d).—A mixture of 1.78 g (6.0 mmoles) of the iminoestrone (**1a**), 1.15 g (6.6 mmoles) of *p*-chlorobenzoyl chloride, and 2.54 g (24 mmoles) of anhydrous sodium carbonate in 80 ml of methylene chloride was stirred vigorously at room temperature for 1 hr. Water (25 ml) was added and stirring continued for 2 hr. The layers were separated and the organic phase was washed thoroughly with water, dried, treated with Darco, and evaporated to an oil which readily crystallized on trituration with ether. The product was washed with a small amount of ether and dried to give 2.57 g (98%) of a white solid, mp 213–233°, which gave a single symmetrical spot by tlc.

Product from a similar run was crystallized twice from acetone to give material with mp 200–223°; λ_{max} 308 mμ (ε 7000); $[\alpha]D$ −162°; ν_{max}^{KBr} 1634 cm^{-1} (amide CO + aromatic bands); nmr 7.25–7.66 (m, *p*-chlorobenzoyl protons), 6.30 (m, C-2 H), 5.74 (m, C-4 H), 3.56 (s, OCH_3), 1.08 ppm (s, C-18 CH_3).

Anal. Calcd for $C_{26}H_{26}ClNO_3$ (435.93): C, 71.64; H, 6.01; N, 3.21; Cl, 8.13. Found: C, 71.29; H, 6.06; N, 3.14; Cl, 8.21.

3-Methoxy-1,11α-methyliminoestra-1,3,5(10)-trien-17-one (1e).—To a solution of 5.0 g (16.8 mmoles) of the iminoestrone (**1a**) in 150 ml of 20% dimethylformamide in benzene (dried over molecular sieves) was added 920 mg of a 54.7% dispersion of sodium hydride (21 mmoles) in mineral oil. The mixture was stirred for 5 min at 40°, then 10.4 ml (23.9 g, 168 mmoles) of methyl iodide was added and stirring continued at 35–40° for 1 hr.

The mixture was treated with a few drops of methanol to decompose any unreacted sodium hydride, and then was washed with water, dried, and evaporated to give 3.08 g of a cream solid. The crude product was chromatographed on Florisil (250 g), using 10% ethyl acetate–hexane as eluent to give 2.4 g (46% yield) of product. A single crystallization from methylene chloride–ether gave 2.2 g: mp 166–168°; λ_{max} 214, 250 (sh), 293 mμ (ε 31,100, 5000, 4040); $[\alpha]D$ +67°; ν_{max}^{KBr} 1125 (OCH_3), 831 cm^{-1} (aromatic CH); nmr 6.08 (m, C-2 H, C-4 H), 3.73 (s, OCH_3), 2.65 (s, NCH_3), 1.00 ppm (s, C-18 CH_3).

Anal. Calcd for $C_{20}H_{25}NO_2$ (311.41): C, 77.13; H, 8.09; N, 4.50. Found: C, 77.22; H, 8.34; N, 4.48.

3-Methoxy-1,11-methyliminoestra-1,3,5(10),9(11)-tetraen-17-one (2c).—A mixture of 1.4 g (4.5 mmoles) of the dihydro compound (**1e**), 450 mg of 10% palladium on carbon (Baker & Co., Inc.), and 30 ml of xylene was stirred and refluxed for 1.5 hr.

The mixture was filtered through 25 g of Magnesol which was then washed thoroughly with hexane; the product was desorbed with methylene chloride (~300 ml). Evaporation of the methylene chloride filtrate followed by trituration of the resulting oil with ether gave 1.25 g (91% yield) of colorless crystals, mp 143–150°.

The product was crystallized twice from methylene chloride–ether to give 1.03 g: mp 150–152°; λ_{max} 232, 281, 300 mμ (sh) (ε 36,500, 5870, 4000); $[\alpha]D$ +236°; ν_{max}^{KBr} 812 cm^{-1} (aromatic CH); nmr 6.54 (m, C-2 H, C-4 H), 3.82 (s, OCH_3), 3.50 (s, NCH_3), 1.17 ppm (s, C-18 CH_3).

Anal. Calcd for $C_{20}H_{23}NO_2$ (309.39): C, 77.64; H, 7.49; N, 4.53. Found: C, 77.29; H, 7.41; N, 4.80.

1,11(*p*-Chlorobenzoyl)imino-3-methoxyestra-1,3,5(10),9(11)-tetraen-17-one (2b).—To a stirred solution of 1.15 g (2.63 mmoles) of 1,11α-(*p*-chlorobenzoyl)imino-3-methoxyestra-1,3,5(10)-trien-17-one (**1d**) in 25 ml of methylene chloride was added a solution of 626 mg (2.76 mmoles) of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in 30 ml of methylene chloride. The mixture was stirred for 10 min at room temperature and then was filtered through 8 g of Magnesol followed by washing with 100 ml of methylene chloride. Evaporation of the filtrate gave an oil which crystallized on trituration with ether to afford 1.09 g (96%) of yellow crystals, mp 230–243°. The product was crystallized twice from acetone to give 974 mg: mp 248–250°; λ_{max} 230, 262 mμ (ε 23,000, 18,200); $[\alpha]D$ +165°; ν_{max}^{KBr} 1667 cm^{-1} (amide CO).

Anal. Calcd for $C_{26}H_{24}ClNO_3$ (433.92): C, 71.97; H, 5.57; N, 3.23; Cl, 8.17. Found: C, 72.26; H, 5.78; N, 3.41; Cl, 8.33.

4-Hydroxy-1,11-imino-3-methoxyestra-1,3,5(10),9(11)-tetraen-17-one (3).—A solution of potassium nitrosodisulfonate (1.40 g, 5.2 mmoles) and anhydrous sodium acetate (615 mg, 7.5 mmoles) in 75 ml of water was added to a solution of 750 mg (2.52 mmoles) of 1,11α-iminoestrone 3-methyl ether (**1a**) in 75 ml of acetone and the mixture was stirred at room temperature for 30 min. Water (50 ml) and acetic acid (1.0 ml) were added and stirring was continued for an additional 30 min.

The mixture was extracted with chloroform and the extract was washed with water, dried, and evaporated to a dark oil. The oil was dissolved in benzene (~50 ml) and washed with 1 *N* HCl and then with water. The resulting benzene solution was dried and placed on a silica gel column (70 g). Elution with 15% acetone–hexane gave 50 mg (6.7% yield) of 1,11-imino-3-methoxyestra-1,3,5(10),9(11)-tetraen-17-one (**2a**, identical with an authentic sample by infrared spectra and tlc). Further elution of the column with 20% acetone–hexane gave 426 mg (54%) of slightly impure product which on crystallization from methylene chloride–benzene yielded 332 mg of a pale tan solid: mp 240–260°, pure by tlc; λ_{max} 223, 280, 300 (sh), 306 mμ (ε 23,400, 6200, 7150, 7300); ν_{max}^{KBr} 3401 cm^{-1} (OH + NH); $[\alpha]D$ +247°; nmr (in $CDCl_3$ and DMSO-d_6), 9.21 (m, OH), 6.66 (m, C-2 H, NH), 3.80 (s, OCH_3), 1.15 ppm (s, C-18 CH_3).

Anal. Calcd for $C_{19}H_{21}NO_3$ (311.37): C, 73.29; H, 6.80; N, 4.50. Found: C, 73.63; H, 6.91; N, 4.52.

1,11α-(*p*-Chlorobenzoyl)imino-3-methoxy-16,17-secoestra-1,3,5(10)-triene-16,17-dioic Acid (4).—To a well-stirred solution of 2.53 g (5.8 mmoles) of 1,11α-(*p*-chlorobenzoyl)imino-3-methoxyestra-1,3,5(10)-trien-17-one (**1d**) in 252 ml of purified dioxane plus 28 ml of water, at room temperature, was added over 45 min a solution of 3.8 g (15 mmoles) of iodine in 60 ml of purified dioxane. Simultaneously, from a separate funnel was added 60 ml of 2 *N* aqueous sodium hydroxide. The mixture was stirred at room temperature for 4 hr, then concentrated to approximately 225 ml and diluted with 500 ml of water, and filtered through a bed of Celite. The residue on the Celite was washed with water and methylene chloride and the total filtrate was extracted with methylene chloride and then with ether. The resulting aqueous phase was acidified with 60 ml of 2 *N* hydrochloric acid and extracted with ether. The ether extract was washed with 10% sodium thiosulfate solution and with water. The solution was dried and evaporated to give 2.27 g of a crude product which was chromatographed on silica gel (150 g) using 20% acetone–hexane as the eluting solvent. Crystallization of the product from methylene chloride–ether yielded 1.13 g of white crystals which were pure by tlc.

Impure fractions from the column chromatography and the mother liquor from the above crystallization were chromatographed again and crystallized to give an additional 54 mg of product (1.18 g total, 42% yield). A final crystallization from methylene chloride–ether gave 1.06 g, mp 167–180°. The product was homogeneous by tlc but elemental analysis indicated that it was hydrated: λ_{max} 307 mμ (ε 7150); $[\alpha]D$ −150° (pyridine); ν_{max}^{KBr} 2924 (carboxyl OH), 1709 (carboxyl CO, dimer), 1621 cm^{-1} (amide CO + aromatic band); nmr (in DMSO-d_6), 7.53 (s, *p*-chlorobenzoyl protons), 6.34 (m, C-2 H), 5.85 (m, C-4 H), 3.54 (s, OCH_3), 1.10 ppm (s, C-18 CH_3).

Anal. Calcd for $C_{26}H_{26}ClNO_2 \cdot {}^1/_2H_2O$ (492.93): C, 63.35; H, 5.52; N, 2.84; Cl, 7.19. Found: C, 63.39; H, 5.45; N, 3.01; Cl, 7.55.

1,11-(*p*-Chlorobenzoyl)imino-3-methoxy-16,17-secoestra-1,3,5(10),9(11)-tetraene-16,17-dioic Acid (5).—To a solution of 710 mg (1.47 mmoles) of the seco diacid **4** in 50 ml of methylene chloride was added a solution of 355 mg (1.56 mmoles) of DDQ in 30 ml of methylene chloride, in one portion, and the mixture was stirred at room temperature for 1 hr.

The mixture was filtered and the filtrate was evaporated to a yellow oil which was chromatographed on silica gel (50 g). The product was eluted with 20% acetone–hexane and crystallized from ether to give 547 mg (77% yield) of product. Recrystallization from ether gave 456 mg of a pale yellow solid: mp 202–204°; pure by tlc; λ_{max} 230 (sh), 260 mμ (ε 22,200, 20,700); $[\alpha]D$ −59° (pyridine); ν_{max}^{KBr} 2941 (carboxyl OH), 1709, 1687 cm^{-1} (carboxyl CO); nmr (in DMSO-d_6), 7.63 (s, *p*-chlorobenzoyl protons), 6.61 (m, C-2 H), 6.28 (m, C-4 H), 3.58 (s, OCH_3), 1.17 ppm (s, C-18 CH_3).

Anal. Calcd for $C_{26}H_{24}ClNO_6$ (481.91): C, 64.79; H, 5.02;

N, 2.91; Cl, 7.36. Found: C, 64.96; H, 5.19; N, 3.01; Cl, 7.68.

4,5-(*p*-Chlorobenzoyl)imino-9,10-dihydro-7-methoxy-2-methylphenanthrene-1-acetic Acid (6a).—To a solution of 50 mg (0.104 mmole) of the diacid **5** in 10 ml of methylene chloride was added 2 equiv (47 mg, 0.207 mmole) of DDQ in 5 ml of methylene chloride and the mixture stirred at room temperature for 1.5 hr.

The mixture was filtered and the filtrate was purified by preparative tlc using benzene–dioxane–acetic acid 90:25:6 as the developing solvent. Three main components were isolated: 21 mg (50% yield) of product (R_f 0.54), 5 mg of starting material (R_f 0.39), and 12 mg of a slightly more polar by-product (R_f 0.31).

The main product (R_f 0.54) had mp 195–220°; λ_{max} 232, 290 mμ (ε 38,600, 18,200); ν_{max}^{KBr} 2941 (carboxyl OH), 1695 (carboxyl CO), 1667 cm^{-1} (amide CO); nmr (in DMSO-d_6), 7.65 (s, *p*-chlorobenzoyl protons), 6.81 (s, C-3 H), 6.73 (m, C-6 H), 6.38 (m, C-8 H), 3.63 (s, OCH_3 + CH_2COO), 3.12 (s, C-9 H_2 + C-110 H_2), 2.25 ppm (s, C-2 CH_3); mass spectrum, *m/e* 433 [M$^+$, calcd for $C_{25}H_{20}ClNO_4$, 433], 389 [M − CO_2], 139 [base peak, *p*-ClC_6H_4CO].

Methyl 4,5-(*p*-Chlorobenzoyl)imino-9,10-dihydro-7-methoxy-2-methylphenanthrene 1-Acetate (6b).—To a suspension of 40 mg (0.092 mmole) of the acid **6a** in 8 ml of methanol were added several portions of ethereal diazomethane. The solution was acidified with acetic acid, washed with water, and evaporated.

The crude product was purified by preparative tlc using cyclohexane–ethyl acetate (70:30) as the developing solvent to give 37 mg (90%) of the methyl ester: mp 173–177°; λ_{max} (neutral) 231, 270 (sh) 290 mμ (ε 44,600, 17,800, 20,800); λ_{max} (basic) 244, 260 (sh), 305, 317 mμ (sh) (ε 56,400, 25,100, 11,700, 10,400); ν_{max}^{KBr} 1733 (carbomethoxyl CO), 1675 cm^{-1} (amide CO); nmr 7.33–7.67 (m, *p*-chlorobenzoyl protons), 6.90 (s, C-3 H), 6.61 (s, C-6 H + C-8 H), 3.68 (s, CH_2COOCH_3), 3.63 (s, OCH_3), 3.17 (s, C-9 H_2 + C-10 H_2), 2.30 ppm (s, C-2 CH_3); mass spectrum, *m/e* 447 [M$^+$, calcd for $C_{25}H_{20}ClNO_4$, 447], 388 [M − $COOCH_3$], 374 [M − CH_2COOCH_3], 249 [M − ($COOCH_3$ + *p*-ClC_6H_4CO)], 235 [M − (CH_2COOCH_3 + *p*-ClC_6H_4CO)].

Methyl 9,10-Dihydro-4,5-imino-7-methoxy-2-methylphenanthrene 1-Acetate (7).—To a solution of the methyl ester (**6b**, 21 mg, 0.048 mmole) in 10 ml of methylene chloride was added 84 mg (1.5 mmoles) of potassium hydroxide dissolved in 25 ml of methanol. The solution was allowed to stand at room temperature for 1 hr, then acidified with acetic acid, and evaporated in the presence of toluene. The resulting residue was dissolved in methylene chloride, filtered through Celite, and evaporated to a glass (19 mg) which was purified by preparative tlc (cyclohexane–ethyl acetate 70:30) to give 13 mg (91%) of pale tan crystals: mp 130–140°; λ_{max} 244, 260 (sh), 305, 317 mμ (sh) (ε 31,500, 17,300, 8300, 7100); $\nu_{max}^{CHCl_3}$ 3448 (NH), 1724 (carbomethoxyl CO), 1139 cm^{-1} (OCH_3); nmr (in DMSO-d_6), 10.4 (m, NH), 6.95 (s, C-3 H), 6.67 (m, C-6 H), 6.50 (m, C-8 H), 3.75, 3.70 (s, s, CH_2COOCH_3), 3.55 (s, OCH_3), 3.14 (s, C-9 H_2 + C-10 H_2), 2.35 ppm (s, C-2 CH_3).

The Stereochemistry of the Cleavage of a Steroid 4,4-Dimethyl-3,4-seco Lactone

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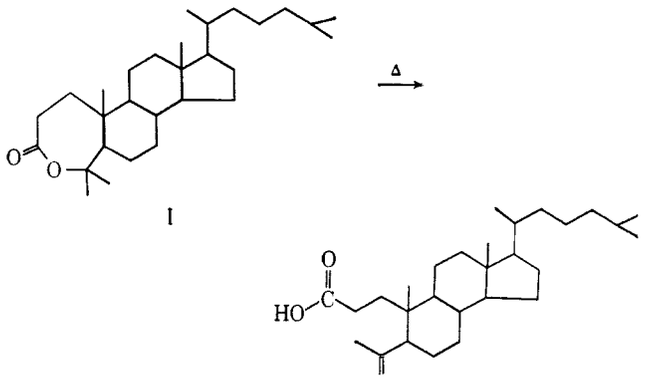
It has been reported recently[1] that the lactone I, obtained by the Baeyer–Villiger oxidation of 4,4-dimethylcholestanone, is readily pyrolized to the unsaturated acid II.



I

II

The recent interest in the detailed mechanism and stereochemistry of the biological synthetic pathways to steroids and terpenes[2] made us feel that this reaction, if stereospecific, could serve as the basis for the chemical degradation of steroid precursors, such as lanosterol, or of other triterpenes in order to verify the biogenesis of each C-4 methyl group in these substances. Accordingly we have carried out a series of reactions to determine to what extent each of the C-4 methyl groups in I are converted to the methylene and methyl portions of the isopropenyl group in II.

4-Methylcholestenone (III)[1,3] was alkylated with a slight excess of trideuteriomethyl iodide in the presence of potassium *t*-butoxide and *t*-butyl alcohol. It has been shown that when 4-methylcholesten-3-one is ethylated under basic conditions, the incoming alkyl group is nearly exclusively introduced into the 4α position.[4] Since the size of the alkylating agent does not materially effect the stereospecificity of the alkylation reaction,[5] the product of our trideuteriomethylation reaction was therefore 4β-methyl-4α-trideuteriomethyl-5-cholesten-3-one (IV).

Catalytic reduction of ketone IV with hydrogen on platinum in ethyl acetate containing a trace of perchloric acid smoothly gave 4β-methyl-4α-trideuteriomethyl-5α-cholestan-3β-ol (V). The 100-Mc nmr spectrum of this substance was identical with that of the unlabeled alcohol with the exception of the total absence[6] of the sharp signal at 96.5 cps (downfield from TMS) present in undeuterated V which can be assigned to the 4α-methyl group. This evidence proves that the original assignment[7] of the nmr signals for the 4α- and 4β-methyl groups in triterpene 3β alcohols was reversed and that the assignments made by Hemmert, *et al.*,[8] are correct.

Oxidation of the 3β alcohol V with chromium trioxide in acetone gave the deuterated 4,4-dimethylcholestan-3-one (VI) which was oxidized in chloroform solution with *m*-chloroperbenzoic acid to the 4aα-trideuteriomethyl lactone VII. Pyrolysis of this lactone at 205° was complete after 50 min and the

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