Heterocyclic Steroids. Part II.[1] Synthesis of (±)-8-Hydroxy-3-methoxy-11-aza-18-norestra-1,3,5(10),9(11)-tetraen-17-one and Related Compounds

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5-Oxo-2-(1,2,3,4-tetrahydro-6-methoxy-2-naphthyl)cyclopent-1-enylacetic acid (II), readily available from 2-acetyl-1,2,3,4-tetrahydro-6-methoxynaphthalene (I), was hydrogenated and then oxidised with chromic acid to give the dioxo-acid (IV). By a modified Curtius rearrangement this afforded (±)-9(11)-didehydro-8-hydroxy-11-aza-18-norestrone 3-methyl ether (IX), the hydroxy-group being presumably introduced through autoxidation. In contrast, similar treatment of the 13-methyl acids (V) and (VI) of the natural series gave the 3-methyl ethers of 9(11)-didehydro-11-aza-estrone (X) and -17β-estradiol (XI), which do not undergo oxidation in air.

RECENTLY, we have synthesised a 6,15-diazaequilenin derivative [1] by use of a modified Curtius rearrangement.[2] The reaction has now been employed for the total synthesis of an (±)-11-aza-18-norestrone derivative (IX) (see ref. 3 for a similar partial synthesis). The method is capable of providing a direct route to 11-aza-estrogens [4] from easily accessible materials and affords useful intermediates for the synthesis of 9,11-seco-steroids, a number of which have been synthesised lately [5]

[1] D. Nasipuri and S. K. Ghosh, *J.C.S. Perkin I*, 1974, 2720 is regarded as Part I.

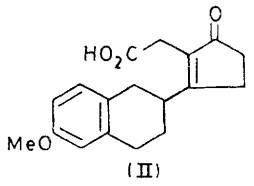
[2] J. G. Morgan, K. D. Berlin, N. N. Durham, and R. W. Chesnut, *J. Org. Chem.*, 1971, **36**, 1599.

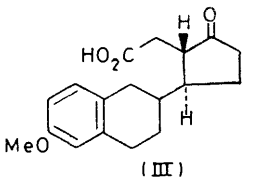
[3] P. Yu. Badanova and K. K. Pivnitakii, *Zhur. obshchei Khim.*, 1971, **41**, 242 (*Chem. Abs.*, 1971, **75**, 36,455q).

[4] For a review, see R. I. Blickenstaff, A. C. Ghosh, and G. C. Wolf, ' Total Synthesis of Steroids,' Academic Press, New York, 1974.

[5] J. H. Dygos and L. J. Chinn, *J. Org. Chem.*, 1973, **38**, 4319; 1975, **40**, 685; L. J. Chinn, J. H. Dygos, S. E. Mares, R. L. Aspinall, and R. E. Ranney, *J. Medicin. Chem.*, 1974, **17**, 351; N. S. Crossley and R. Dowell, *J. Chem. Soc.* (*C*), 1971, 2496.

in view of their modified biological activity. Some observations on the autoxidation of imines resulting from the Curtius reaction are also recorded.


(II)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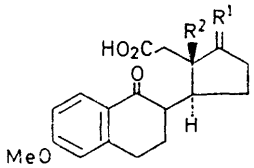
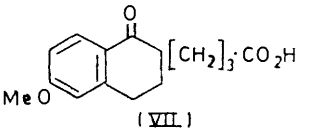
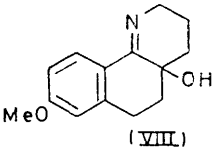
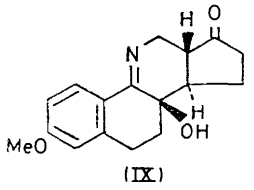
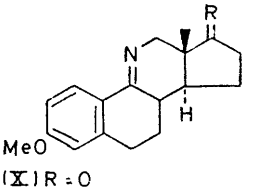

(IV) R^1 = O, R^2 = H
(V) R^1 = O, R^2 = Me
(VI) R^1 = H, OAc, R^2 = Me

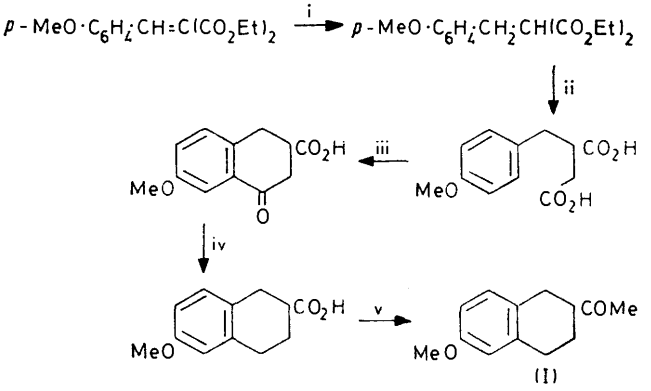

(VII)


(VIII)


(IX)


(X) R = O
(XI) R = H, OH

2-Acetyl-1,2,3,4-tetrahydro-6-methoxynaphthalene (I) was prepared from *p*-anisaldehyde through the sequence of reactions shown in Scheme 1 in an overall yield of 40%. The ketone was converted into 5-oxo-2-(1,2,3,4-tetrahydro-6-methoxy-2-naphthyl)cyclopent-1-enylacetic acid (II) through its furfurylidene derivative.[6] The methyl ester was reduced catalytically and the *trans*-isomer, obtained as the major product [7] was hydrolysed to (±)-3-methoxy-18-nor-17-oxo-9,11-seco-estra-1,3,5(10)-trien-11-oic acid (III). This was oxidised with chromic acid to the tetralone derivative (IV), obtained in moderate yield but easily separable from the reaction mixture. The position of the ketonic group was confirmed by spectral data (see Experimental section) and also by a model experiment in which γ-(1,2,3,4-tetrahydro-6-methoxy-2-naphthyl)butyric acid was oxidised to the corresponding tetralone (VII). Both the keto-acids (IV) and (VII) were submitted to a modified Curtius reaction as described before.[1] (±)-8-Hydroxy-3-methoxy-11-aza-18-norestra-1,3,5,9(11)-tetraen-17-one (IX) and 2,3,4,4a,5,6-hexahydro-4a-hydroxy-8-methoxybenzo[*h*]quinoline (VIII) were obtained in 36



SCHEME 1 Reagents: i, H_2, Pd–C; ii, NaOEt, $ClCH_2{\cdot}CO_2Et$, hydrolysis and heat; iii, heating with Ac_2O followed by $AlCl_3$; iv, $NH_2{\cdot}NH_2$ and KOH or H_2, Pd–C in AcOH–HCl; v, $(EtO)MgC(CO_2Et)_2$ on the derived acid chloride and hydrolysis

and 50% yields, respectively. The insertion of the hydroxy-group is not surprising; many imines are sensitive to oxidation and are converted into hydroperoxides on exposure to air.[8] The latter ordinarily decompose to give secondary products including β-hydroxy-imines [as (VIII) and (IX)] in contact with solvents.[9] We were, however, unable to detect any hydroperoxide or other by-products (such as cyclic oxo-lactams) in the above reactions. Further study is necessary to show whether the hydroxy-derivatives are primary oxidation products [10] or are merely formed by spontaneous decomposition of the hydroperoxides.

The structure of the aza-steroid (IX) was supported by i.r., n.m.r., and mass spectra, and by elemental analysis. The mass spectrum showed prominent peaks at *m/e* 285 (M^+, 100%), 268 (17, $M - OH$), 267 (14, $M - H_2O$), 266 (12, $M - H_2O - H$), 212 (41, $M - OH - CH_2{\cdot}$: $CH_2 - CO$), 203 (80), 175 (84), 174 (53), and 160 (24) (Scheme 2). The peak at *m/e* 203 corresponds to the fragment (XII), which confirms the position of the hydroxy-group. The peak at *m/e* 175 possibly arises through elimination of OH, hydrogen migration, and extrusion of $C_6H_5O{\cdot}$ [from C(12—17)].

The unsaturated oxo-acid [as (II)] could, in principle, undergo reductive methylation [11] as reported in an analogous case,[12] and the product (usually a mixture of

[6] R. Robinson, *J. Chem. Soc.*, 1938, 1390; A. Koebner and R. Robinson, *ibid.*, p. 1994; M. M. Coombs and T. S. Bhatt, *J.C.S. Perkin I*, 1973, 1251; V. M. Kapoor and A. M. Mehta, *ibid.*, p. 2420.

[7] L. J. Chinn, E. A. Brown, R. A. Mikulec, and R. B. Garland, *J. Org. Chem.*, 1962, **27**, 1733; Y. Amiel, A. Loffler, and D. Ginsburg, *J. Amer. Chem. Soc.*, 1954, **76**, 3625.

[8] See A. G. Cook, 'Enamines: Synthesis, Structure, and Reactions,' Dekker, New York, 1969, p. 285, for references.

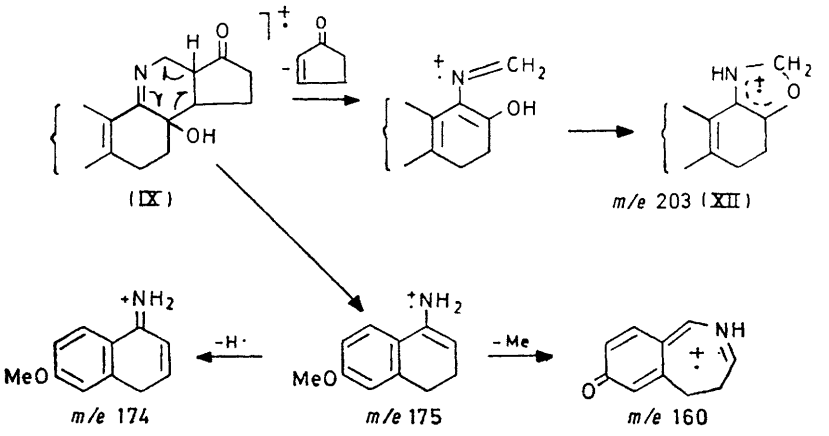
[9] L. A. Cohen and B. Witkop, *J. Amer. Chem. Soc.*, 1955, **77**, 6595.

[10] B. Witkop, *J. Amer. Chem. Soc.*, 1950, **72**, 1428; B. Witkop and J. B. Patrick, *ibid.*, 1951, **73**, 713.

[11] G. Stork, P. Rosen, N. Goldman, R. V. Coombs, and J. Tsuji, *J. Amer. Chem. Soc.*, 1965, **87**, 275.

[12] A. J. Birch and G. S. R. Subba Rao, *Austral. J. Chem.*, 1970, **23**, 547.

stereoisomers [13]) could be used for the synthesis of 9,11-seco-steroids [5] or be oxidised to the dioxo-acid (V). The latter, however, is available in natural configuration by oxidation of estrone methyl ether with chromic acid.[14] The corresponding 17β-acetoxy-derivative (VI) has previously been converted into 11-aza-estrogens by Russian workers.[3] Since the details of this work were not available, we repeated the experiments with the oxo-acid (V) and its 17β-acetoxy-derivative (VI) under our own conditions. In both cases, the 11-aza-steroid [(X) and (XI)] was obtained in *ca.* 50% yield, and each



SCHEME 2

was characterised by n.m.r. and mass spectra. No oxidation of the resulting imines was detected. Apparently, oxygen approaches the molecule from the β-side [*syn* with respect to 13-H and *trans* with respect to 14-H in (IX)] and such attack is prevented in the 13β-methyl aza-steroids (X) and (XI) by a *syn*-methyl interaction. This fixes the configuration of the hydroxy-group in the synthetic compound as in structure (IX) (only one enantiomer is shown). No hydroxylation occurs when the β-carbon atom in the imines carries no hydrogen atom, as in 2,3,4,4a,5,6-hexahydro-4a-methylbenzo[*h*]-quinoline (VIII; Me in place of OH).[15]

EXPERIMENTAL

N.m.r. spectra were measured with a Varian T60 60 MHz spectrometer for solutions in [^{2}H]chloroform unless otherwise stated, with tetramethylsilane as internal standard. Mass spectra were determined with a Hitachi RMU-6L spectrometer at 80 eV by using the direct inlet system. M.p.s were taken for samples in open capillaries in a sulphuric acid bath. Petroleum refers to the fraction of b.p. 60—80°. Organic extracts were dried over anhydrous sodium sulphate. The homogeneity of compounds was checked by t.l.c. on silica gel.

[13] E. G. Brain, F. Cassidy, M. F. Constantine, J. C. Hanson, and J. D. Tidy, *J. Chem. Soc.* (*C*), 1971, 3846.
[14] R. C. Cambie and T. D. R. Manning, *J. Chem. Soc.* (*C*), 1968, 2603; R. C. Cambie, V. F. Carlisle, C. J. LeQuesne, and T. D. R. Manning, *ibid.*, 1969, 1234.
[15] D. Nasipuri and S. K. Ghosh, unpublished data; see also ref. 2.

1,2,3,4-*Tetrahydro*-6-*methoxy*-4-*oxonaphthalene*-2-*carboxylic Acid*.—The oxo-acid was prepared essentially by a known procedure,[16,17] as shown in Scheme 1: m.p. 158—159° (from ethyl acetate) (lit.,[16] m.p. 149—151°) (Found: C, 65.8; H, 5.9. Calc. for $C_{12}H_{12}O_4$: C, 65.5; H, 5.4%), $\nu_{max.}$ (Nujol) 1 700 and 1 660 cm^{-1}.

1,2,3,4-*Tetrahydro*-6-*methoxynaphthalene*-2-*carboxylic Acid*.—The foregoing oxo-acid was reduced by the Huang-Minlon procedure [16] as well as by hydrogenation over 10% palladium–charcoal in acetic acid containing a few drops of hydrochloric acid. The resulting acid had m.p. 156—157° (from ethyl acetate) (lit.,[16] m.p. 149—150°) (Found: C, 70.1; H, 7.0. Calc. for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8%), $\nu_{max.}$(Nujol) 1 700 cm^{-1}.

2-*Acetyl*-1,2,3,4-*tetrahydro*-6-*methoxynaphthalene* (I).—The foregoing acid (14.4 g, 0.07 mol) was treated with refluxing thionyl chloride (8 ml) for 4 h. Removal of thionyl chloride, left the acid chloride as a crystalline solid, m.p. 77°. To a solution of diethyl ethoxymagnesiomalonate [from magnesium (1.92 g, 0.08 mol), ethyl malonate (12.8 g, 0.8 mol), absolute ethanol (17 ml), dry ether (50 ml), and a drop of carbon tetrachloride (to initiate the reaction) [18]] the acid chloride (14.4 g) in ether (100 ml) was slowly added. The solution was kept refluxing during the addition and until it became too viscous to be stirred. After cooling, the mixture was decomposed with dilute sulphuric acid, the ethereal layer separated, the aqueous solution once extracted with ether, and the combined organic extracts dried and evaporated. The residue was hydrolysed with a refluxing mixture of concentrated sulphuric acid (4 ml), acetic acid (24 ml), and water (16 ml) for 5 h. The usual work-up [18] afforded the *ketone* (I) (11.8 g), b.p. 160° at 0.6 mmHg (Found: C, 76.3; H, 7.9. $C_{13}H_{16}O_2$ requires C, 76.5; H, 7.8%), $\nu_{max.}$ (neat) 1 712 cm^{-1}, τ (CCl_4) 7.80 (s, MeCO); *dinitrophenylhydrazone* (from methanol–ethyl acetate), m.p. 125° (Found: C, 59.1; H, 5.4; N, 14.5. $C_{19}H_{20}N_4O_5$ requires C, 59.4; H, 5.2; N, 14.6%).

2-*Furfurylideneacetyl*-1,2,3,4-*tetrahydro*-6-*methoxynaphthalene*.—The ketone (I) (2.04 g, 0.01 mol) was condensed

[16] J. Jacques and A. Horeau, *Bull. Soc. chim. France*, 1950, 512.
[17] R. D. Haworth, B. Jones, and Y. M. Way, *J. Chem. Soc.*, 1943, 10; K. N. Campbell, J. A. Cella, and B. K. Campbell, *J. Amer. Chem. Soc.*, 1953, **75**, 4681.
[18] G. A. Reynolds and C. R. Hauser, *Org. Synth.*, Coll. Vol. IV, 1963, 708.

with 2-furaldehyde (1.2 g) in the presence of methanolic 4% sodium methoxide (10 ml). After 24 h at room temperature, the pale yellow crystals (2.7 g) were collected and recrystallised from ethanol to give light yellow *plates*, m.p. 108° (Found: C, 76.7; H, 6.3. $C_{18}H_{18}O_3$ requires C, 76.6; H, 6.4%), $\nu_{max.}$ (Nujol) 1 682 and 1 610 cm^{-1}.

4,7-Dioxo-7-(1,2,3,4-tetrahydro-6-methoxy-2-naphthyl)heptanoic Acid.—The above furfurylidene derivative (2.4 g) was heated under reflux with concentrated hydrochloric acid (9 ml) and ethanol (40 ml) for 18 h. The tarry material obtained after removal of ethanol was boiled with a mixture of concentrated hydrochloric acid (25 ml), glacial acetic acid (30 ml), and water (65 ml) for 2—3 h. The hot solution was filtered through glass wool and the filtrate was set aside. The process was repeated several times and the combined filtrates on cooling afforded the *dioxo-acid* (1.35 g). Recrystallisation from aqueous methanol gave white plates, m.p. 99—101° (Found: C, 67.5; H, 7.2. $C_{18}H_{22}O_5$ requires C, 67.9; H, 6.9%), $\nu_{max.}$ (Nujol) 1 700—1 730br cm^{-1}.

5-Oxo-2-(1,2,3,4-tetrahydro-6-methoxy-2-naphthyl)cyclopent-1-enylacetic Acid (II).—The preceding dioxo-acid (1.2 g) was taken up in aqueous 2% potassium hydroxide (100 ml) and warmed at 95 °C for 1.5 h. The solution was cooled and acidified with concentrated hydrochloric acid. The pale yellow crystalline solid obtained was filtered off, washed with water, and dried to give the *acid* (II) (1.07 g, 95%), m.p. 170°. Recrystallisation from methanol afforded pale yellow needles, m.p. 172—173° (Found: C, 71.9; H, 6.8. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%), $\nu_{max.}$ (Nujol) 1 720 and 1 700 cm^{-1}. The *methyl ester*, prepared by treatment with refluxing methanolic 3% hydrogen chloride formed plates, m.p. 91° (methanol) (Found: C, 72.7; H, 7.3. $C_{19}H_{22}O_4$ requires C, 72.6; H, 7.0%), τ 2.90—3.34 (3 H, m, ArH), 6.17 (3 H, s, CO_2Me), 6.27 (3 H, s, OMe), 6.70 (2 H, s, $CH_2{\cdot}CO_2Me$), 6.90—7.70 (9 H, m, 4 × CH_2 + CH), and 8.08 (2 H, m, 4-H_2).

(±)-3-Methoxy-17-oxo-18-nor-9,11-secoestra-1,3,5(10)-trien-11-oic Acid (III).—The above methyl ester (3.14 g) was dissolved in methanol (50 ml) and shaken with 10% palladium–charcoal (500 mg) in hydrogen. The catalyst was removed and the filtrate was treated with sodium methoxide [from sodium (50 mg) and methanol (2 ml)]. The solvent was removed (steam-bath) and the residual gum (3.1 g) was chromatographed over alumina. A main fraction (2.9 g) showing a single spot on t.l.c. was isolated. This was hydrolysed by heating with ethanolic 10% potassium hydroxide to furnish a *keto-acid* as a gum which, from analogy,[7] was assigned the *trans*-structure (III) (Found: C, 71.3; H, 7.6. $C_{18}H_{22}O_4$ requires C, 71.5; H, 7.3%), $\nu_{max.}$ ($CHCl_3$) 1 745 and 1 715 cm^{-1}.

(±)-3-Methoxy-9,17-dioxo-18-nor-9,11-secoestra-1,3,5(10)-trien-11-oic Acid (IV).—The keto-acid (III) (3.0 g, 0.01 mol) was dissolved in glacial acetic acid (11 ml) and a solution of chromic acid (1.8 g, 0.016 mol) in acetic acid (6 ml) and water (0.8 ml) was added in portions during 4h with stirring and cooling (ice–water). The green solution was kept in the refrigerator overnight, then diluted with cold water, and thoroughly extracted with ethyl acetate. The gum obtained by removal of solvent was triturated with ether to give the *tetralone derivative* (IV) as a white solid (1.1 g). Recrystallisation from ethyl acetate gave nodules (0.62 g, 20%), m.p. 188—189° (Found: C, 68.1; H, 6.5%; M^+, 316. $C_{18}H_{20}O_5$ requires C, 68.4; H, 6.3%; *M*, 316.), $\nu_{max.}$ (KBr) 1 742, 1 712, and 1 670 cm^{-1}, ^1H n.m.r. data in agreement with the structure.

[19] W. E. Bachmann and D. G. Thomas, *J. Amer. Chem. Soc.*, 1941, **63**, 598.

(±)-8-Hydroxy-3-methoxy-11-aza-18-norestra-1,3,5,9(11)-tetraen-17-one (IX).—The keto-acid (IV) (0.41 g, 1.3 mmol) was dissolved in anhydrous acetone (60 ml) and cooled to −5 °C. Triethylamine (0.202 g, 2 mmol) was added under nitrogen, followed by ethyl chloroformate (0.217 g, 2 mmol), and the mixture was stirred in the cold for 30 min. Sodium azide (0.195 g, 3 mmol) in water (1 ml) was dropped in and stirring was continued for 2 h at 0 °C. The mixture was poured into ice–water to precipitate the azide as a gum, which was taken up in chloroform and dried.

The residue (0.41 g) left after removal of chloroform (during which partial decomposition of the azide took place) was heated in toluene (10 ml) on a steam-bath for 1 h. Toluene was removed under reduced pressure and the crude isocyanate (0.40 g) was boiled with a mixture of glacial acetic acid (3.5 ml), concentrated hydrochloric acid (3.5 ml), and water (3.5 ml) for 20 h under nitrogen. The cooled solution was diluted with water, extracted thoroughly with ether, and then neutralised with aqueous 10% sodium hydrogen carbonate. The liberated gum was taken up in ether and dried, and the solvent was removed. The residue (0.160 g) solidified on scratching and was adsorbed on an alumina column. Elution with chloroform furnished a white amorphous powder (136 mg), m.p. 134—138°, which was recrystallised from benzene to give *(±)-8-hydroxy-3-methoxy-11-aza-18-norestra-1,3,5(10),9(11)-tetraen-17-one* (IX), m.p. 136—138° (Found: C, 71.5; H; 6.7; N, 5.1. $C_{17}H_{19}NO_3$ requires C, 71.6; H, 6.7; N, 4.9%), $\nu_{max.}$ (Nujol) 3 500—3 200, 1 755, 1 740sh, 1 643w, and 1 610 cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 3 500, 1 760, and 1 630 cm^{-1}, $\lambda_{max.}$ (EtOH) 209 (log ε 4.24), 225 (4.10), and 275 nm (4.06), τ (100 MHz) 2.00 (1 H, d, *J* 9 Hz, 1-H), 3.20 (1 H, 2d, *J* 9 and 3 Hz, 2-H), 3.37 (1 H, d, *J* 3 Hz, 4-H), 6.04 (2 H, m, 12-H_2), 6.18 (3 H, s, OMe), 6.92 (1 H, m, 13-H), 7.22 (2 H, m, 6-H_2), 7.72 (2 H, m, 16-H_2), 7.95—8.26 (5 H, m, 2 × CH_2 + CH), and 8.50 (1 H, s, OH, exchangeable with D_2O).

γ-(1,2,3,4-Tetrahydro-6-methoxy-2-naphthyl)butyric Acid.—Methyl 1,2,3,4-tetrahydro-6-methoxy-1-oxonaphthalene-2-carboxylate was alkylated with ethyl γ-bromobutyrate [19] and the product hydrolysed to furnish γ-(1,2,3,4-tetrahydro-6-methoxy-1-oxo-2-naphthyl)butyric acid (VII), m.p. 102—103° (lit.,[19] 101.5—103°). The oxo-acid (2.0 g) was reduced by heating with hydrazine hydrate (5 ml), diethylene glycol (25 ml), and potassium hydroxide (1.8 g) (Huang-Minlon procedure) to give the title *acid* as a crystalline solid (1.7 g) (from ether–petroleum), m.p. 69—70° (Found: C, 72.4; H, 8.3. $C_{15}H_{20}O_3$ requires C, 72.6; H, 8.0%).

Oxidation of γ-(1,2,3,4-Tetrahydro-6-methoxy-2-naphthyl)-butyric Acid.—A solution of chromic acid (1.0 g) in acetic acid (3 ml) and water (1 ml) was added to the preceding tetralin derivative (0.8 g) in acetic acid (6 ml) with stirring during 5 h. The green solution was left at room temperature overnight, then diluted with water, and the product was worked up in the usual way to give the tetralone derivative (VII) (0.5 g), m.p. 100—101°, identical (i.r. spectra and mixed m.p.) with the previous sample.

2,3,4,4a,5,6-Hexahydro-8-methoxybenzo[h]quinolin-4a-ol (VIII).—The oxo-acid (VII) (2.0 g) was converted into the azide (1.56 g), m.p. 45—55°, and the latter decomposed and rearranged according to the procedure already described to furnish the *benzo[h]quinoline* (VIII) as a crystalline solid. Recrystallisation from chloroform afforded white

plates (1.0 g), m.p. 146—147° (Found: C, 72.5; H, 7.3; N, 6.3%; M^+, 231. $C_{14}H_{17}NO_2$ requires C, 72.7; H, 7.4; N, 6.1%; M, 231), $\nu_{max.}$ (KBr) 3 160, 1 640, and 1 600 cm^{-1}, ^1H n.m.r. data as expected.

Oxidation of 3-*Methoxyestra*-1,3,5(10)-*trien*-17-*one* (*Estrone Methyl Ether*).—Estrone methyl ether was oxidised with chromic acid by a modified procedure.[14] The ether (1.0 g) was taken up in glacial acetic acid (12 ml) and chromic acid (0.85 g) in acetic acid (6 ml) and water (2 ml) was added in the cold during 4 h. The mixture was kept in the refrigerator overnight, then diluted with water, and thoroughly extracted with ether. The extract was shaken repeatedly with aqueous sodium hydrogen carbonate. The alkaline solution on acidification afforded a crystalline compound which was filtered off and crystallised from ether to afford the 9,17-dioxo-acid (V) (0.31 g, 27%), m.p. 155—156° (lit.,[14] m.p. 158°) (Found: C, 68.7; H, 6.8%; M^+, 330. Calc. for $C_{19}H_{22}O_5$ requires C, 69.0; H, 6.7%; M, 330), $\nu_{max.}$ ($CHCl_3$) 1 745, 1 710, and 1 675 cm^{-1}.

3-*Methoxy*-11-*azaestra*-1,3,5(10),9(11)-*tetraen*-17-*one* (X).—The preceding oxo-acid (V) (0.66 g) was converted by a previous procedure into its azide, m.p. 137—145°, and then into the 11-*azaestratetraenone* (X) (0.425 g). This was adsorbed on an alumina column, eluted with benzene, and finally recrystallised from benzene–ether to give needles (0.28 g, 50%), m.p. 162—164° (Found: C, 76.3; H, 7.6; N, 5.1%; M^+, 283. $C_{18}H_{21}NO_2$ requires C, 76.3; H, 7.4, N, 4.9%; M, 283), $\nu_{max.}$ (Nujol) 1 730, 1 615, and 1 590 cm^{-1}, τ (100 MHz) 1.92 (1 H, d, J 9 Hz, 1-H), 3.20 (1 H, 2d, J 9 and 3 Hz, 2-H), 3.34 (1 H, d, J 3 Hz, 4-H), 6.11 (2 H, q, J 8 Hz, 12-H_2), 6.17 (3 H, s, OMe), 7.03 (2 H, m, 6-H_2), 7.38—7.67 (2 H, m, 16-H_2), 7.78 (3 H, m, 15-H_2 + 14 + H), 8.22 (3 H, m, 7-H_2 + 8-H), and 9.06 (3 H, s, Me), $\lambda_{max.}$ (EtOH) 260 (log ε 4.03) and 270 nm (4.06).

3-*Methoxyestra*-1,3,5(10)-*trien*-17-*ol*.—Estrone methyl ether (5 g) was dispersed in methanol (150 ml) and to it sodium borohydride (2.5 g) was added in one portion. After being stirred at room temperature for 1 h, the mixture was refluxed for 1 h, cooled, and decomposed with ice–water. The solid was filtered off and recrystallised from aqueous ethanol to give the 17-ol (4.8 g), m.p. 122° (lit.,[20] 120—121°); acetate, m.p. 102° (lit.,[20] 101—102.5°).

3-*Methoxy*-11-*azaestra*-1,3,5(10),9(11)-*tetraen*-17β-*ol* (XI).—The above acetate was oxidised with chromic acid to the oxo-acid (VI), m.p. 146° (lit.,[14] 141—143°) according to the procedure of Cambie *et al.*[14] The oxo-acid (VI) (1.12 g) was submitted to Curtuis reaction as already described giving successively the azide, m.p. 73°, and the 11-*azaestratetraenol* (XI) (0.65 g). The latter was adsorbed on an alumina column, eluted with benzene–ethyl acetate (9:1), and finally crystallised from ethyl acetate to give plates (0.42 g, 50%), m.p. 225—227° (Found: C, 75.5; H, 8.3, N, 5.2%; M^+, 285. $C_{18}H_{23}NO_2$ requires C, 75.8; H, 8.1; N, 4.9%, M, 285), $\nu_{max.}$ (Nujol) 3 100, 1 600, and 1 575 cm^{-1}, τ (100 MHz) 1.98 (1 H, d, J 9 Hz, 1-H), 3.15 (1 H, d, J 9 Hz, 2-H), 3.33 (1 H, s, 4-H), 6.11 (2 H, m, 12-H_2), 6.17 (3 H, s, OMe), 6.50 (1 H, t, J 15 Hz, 17-H), 7.08 (2 H, m, 6-H_2), 7.67—7.90 (3 H, m, CH_2 + CH), 8.11 (1 H, s, OH), 8.33—8.61 (5 H, m, 2 × CH_2 + CH), and 9.20 (3 H, s, Me).

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