# Synthesis of 11α- and 11β-Diethylaminoethyl Ethers of 17α-Ethynylestradiol

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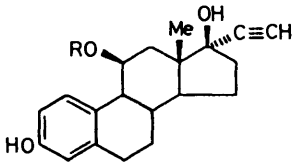
The 11α- and 11β-diethylaminoethyl ethers of 17α-ethynylestradiol have been prepared from the intermediate alcohols (7a) and (7b) by direct alkylation with 2-N,N-diethylaminoethyl bromide hydrobromide followed by hydrogenolysis, deacetalization, and reaction with lithium acetylide. The two 11-diethylaminoethyl ethers of 17α-ethynylestradiol showed no significant estrogenic, anti-estrogenic, or post-coital activity.

THE pronounced estrogenic activity of 11β-methoxy-17α-ethynylestradiol (1) and 11β-ethoxy-17α-ethynylestradiol (2) has been documented.[1,2] As part of a study of the structure–activity relationships of 11-substituted estrogens, we have prepared the previously unreported 11α- and 11β-diethylaminoethyl ethers of 17α-ethynylestradiol, (11a) and (11b), respectively.

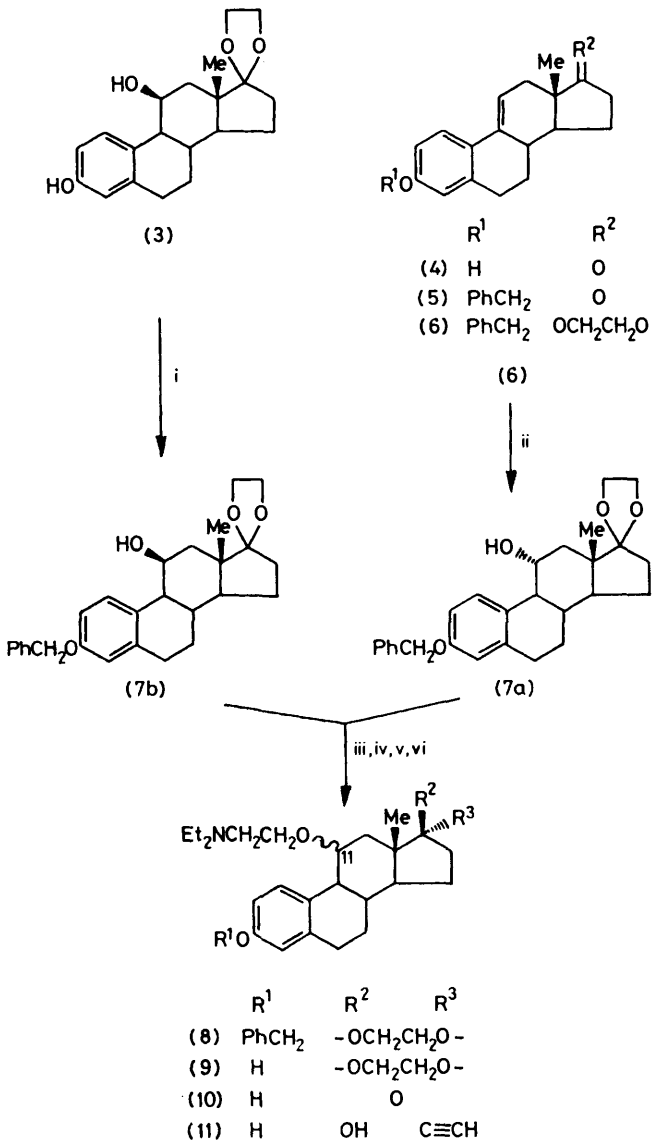


(1) R = Me
(2) R = Et

Initial attempts to prepare the intermediate ether (9b) by reduction of the ester intermediate, 11β-diethylaminoacetoxy-17,17-ethylenedioxyestra-1,3,5(10)-trien-3-ol, under a variety of conditions were unsuccessful. As a result we investigated an alternative approach to prepare the C-11 ethers by direct alkylation of the 11-hydroxy-compound, a method employed in the synthesis of 3,11β,17β-trimethoxyestra-1,3,5(10)-triene.[1] For the 11β-series, the starting diol (3) [3] was first converted into the known [4] 3-benzyl ether (7b).

In the case of the 11α-series, the required intermediate (7a) was obtained from the known [5] $\Delta^{9,11}$-estrone (4). Compound (4) was converted into the benzyl ether (5) by treatment with benzyl bromide and potassium carbonate in dimethylformamide (DMF). The reaction of the ketone (5) with ethylene glycol and toluene-*p*-sulphonic acid monohydrate in benzene led to conversion into the ethylene acetal (6). Hydroboration of (6) with diborane in tetrahydrofuran (THF) followed by oxidation with 30% hydrogen peroxide gave the 11α-alcohol (7a).

The precise conditions necessary for obtaining the C-11 ethers were investigated with the 11β-hydroxy-derivative (7b). Initial attempts to alkylate the alcohol (7b) by 2-*N*,*N*-diethylaminoethyl bromide in the presence of a strong base, *e.g.* sodium hydride, n-butyl-lithium, or lithium hydride, at elevated temperatures (refluxing tetrahydrofuran, refluxing benzene, or dimethylacetamide at 50 °C) gave an extremely poor yield of the desired ether, possibly as a result of the occurrence of a com-



| | $R^1$ | $R^2$ |
|---|---|---|
| (4) | H | O |
| (5) | $PhCH_2$ | O |
| (6) | $PhCH_2$ | $OCH_2CH_2O$ |

| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| (8) | $PhCH_2$ | $-OCH_2CH_2O-$ | |
| (9) | H | $-OCH_2CH_2O-$ | |
| (10) | H | O | |
| (11) | H | OH | C≡CH |

a; 11α
b; 11β

Reagents: i, $K_2CO_3$, $PhCH_2Br$, DMF; ii, $B_2H_6$–THF, $H_2O_2$–NaOH; iii, NaH–THF, $Et_2NCH_2CH_2Br{\cdot}HBr$, 45 °C; iv, $H_2$–Pd–C, EtOH; v, HOAc, THF, $H_2O$; vi, $LiC{\equiv}CH{\cdot}H_2NCH_2CH_2NH_2$, $Me_2SO$

peting base-catalysed dehydrobromination of the aminoalkyl bromide instead of its reaction with the preformed alkoxide. This hypothesis is supported by the fact that after initial preparation of the alkoxide by the action of sodium hydride in refluxing tetrahydrofuran, subsequent low-temperature (10 °C) treatment with the alkyl bromide followed by heating to a maximum temperature of 45 °C gave the alkylamino ether in excellent yield [75% for the 11β-ether (8b) and 90% for the 11α-ether (8a)].

It is known [6,7] that steroidal alcohols can be alkylated by dialkylaminoalkyl chlorides and bromides at elevated temperatures (*e.g.* refluxing xylene). These reactions took place at the 17β-position rather than at the more hindered 11-position, and quite probably the rate of alkylation was fast enough to overcome any deleterious effects caused by a competing base-catalysed elimination of the alkyl halide.

Once the desired ethers had been obtained, the subsequent synthetic steps were carried out by standard methods. The diethers (8a) and (8b) upon hydrogenolysis with palladium on carbon in ethanol afforded the corresponding monoethers (9a) and (9b). Subsequent deacetalization by reaction with acetic acid–tetrahydrofuran–water (3 : 1 : 1) gave the ketones (10a) and (10b), which upon treatment with lithium acetylide–ethylenediamine in dimethyl sulphoxide afforded the desired diethylaminoethyloxy-derivatives (11a) and (11b) of ethynylestradiol.

## EXPERIMENTAL

Unless otherwise stated, m.p.s were determined with a Thomas-Hoover Model 6406-H apparatus; i.r. spectra were recorded for potassium bromide pellets with a Perkin-Elmer 467 spectrophotometer; $^1$H n.m.r. spectra were measured in [$^2$H]chloroform using tetramethylsilane as the internal standard with a Varian EM-390 90 MHz spectrometer; elemental microanalyses were obtained by Midwest Microlab, Ltd., Indianapolis, Indiana; and mass spectra were recorded on a Finigan quadrupole mass spectrometer at either the Southwest Research Institute or The University of Texas Health Science Center at San Antonio. Preparative t.l.c. was carried out on pre-coated silica gel GF plates (20 × 20 cm, 1 000 μm thick) and preparative high-performance liquid chromatography (h.p.l.c.) on a Waters Prep LC/System 500.

3-*Benzyloxy*-11β-(2-N,N-*diethylaminoethyloxy*)-17,17-*ethylenedioxyestra*-1,3,5(10)-*triene* (8b).—Sodium hydride (5.2 g of a 50% dispersion in mineral oil) was suspended in tetrahydrofuran (15 ml) under nitrogen. The mixture was stirred for 5 min and the solvent removed by a pipette. Fresh tetrahydrofuran (100 ml) and a solution of the alcohol (7b) [4] (2.6 g) in tetrahydrofuran (90 ml) were added and the mixture was refluxed for 1 h. The mixture was cooled to 10 °C, 2-*N*,*N*-diethylaminoethyl bromide hydrobromide (1.85 g) added, and the magnetically stirred mixture heated at 45 °C for 16 h. The mixture was cooled to 0 °C and excess of hydride was cautiously decomposed by addition of saturated aqueous sodium sulphate. The organic solution was decanted off and the solid residue triturated several times with ether. The combined organic solution was dried ($Na_2SO_4$), filtered, and concentrated *in vacuo*. The residue was dissolved in chloroform, washed with water, dried ($Na_2SO_4$), filtered, and the solvent removed under reduced pressure to afford an oil (4.0 g) which resisted crystallization. Elution through a short column of silica gel with ethyl acetate followed by methanol gave the crude *ether* (8b) (2.4 g, 75% yield) as a pale yellow oil containing trace impurities (t.l.c.). An analytically pure sample was obtained by preparative t.l.c. (chloroform–methanol, 1 : 1); $\nu_{max.}$ (film): 1 610 and 1 500 cm$^{-1}$; δ 0.88 [6 H, t, *J* 8 Hz, N(CH$_2$*Me*)$_2$], 1.08 (3 H, s, 13-Me), 2.41 [4 H, q, *J* 8 Hz, N(C*H*$_2$Me)$_2$], 3.52br (2 H, m, 11β-OC*H*$_2$CH$_2$NEt$_2$), 3.91 (4 H, m, 17-OCH$_2$CH$_2$O), 4.27 (1 H, m, 11α-H), 5.03 (2 H, s, C*H*$_2$ArH), 6.70 (1 H, s, 4-H), 6.76 (1 H, d of d, *J* 9 and 2 Hz, 2-H), 7.12 (1 H, d, *J* 9 Hz, 1-H), and 7.41 (5 H, m, CH$_2$Ar*H*); m.s. *m/e* 519 ($M^+$) (Found: C, 76.0; H, 8.45. $C_{33}H_{45}NO_4$ requires C, 76.25; H, 8.75%).

11β-(2-N,N-*Diethylaminoethyloxy*)-17,17-*ethylenedioxyestra*-1,3,5(10)-*trien*-3-*ol* (9b).—A mixture of the ether (8b) (2.0 g) and 5% palladium on carbon (2.0 g) under hydrogen (22 lb in$^{-2}$) in absolute ethanol (95 ml) was shaken at ambient temperature in a Parr hydrogenation apparatus for 4 h. The mixture was filtered through Celite, the catalyst washed with additional ethanol (200 ml), and the filtrate concentrated *in vacuo* to the crude *phenol* (9b) (1.46 g, 88% yield) as a foam. Preparative t.l.c. (chloroform–methanol, 1 : 1), and subsequent crystallization from ether gave an analytical sample, m.p. 135—137 °C; $\nu_{max.}$ 3 400, 1 610, and 1 500 cm$^{-1}$; δ 0.86 [6 H, t, *J* 8 Hz, N(CH$_2$*Me*)$_2$], 1.07 (3 H, s, 13-Me), 2.45 [4 H, q, *J* 8 Hz, N(C*H*$_2$Me)$_2$], 3.61br (2 H, m, 11β-OC*H*$_2$CH$_2$NEt$_2$), 3.90 (4 H, m, 17-OCH$_2$CH$_2$O), 4.28 (1 H, m, 11α-H), 6.49 (1 H, s, 4-H), 6.51 (1 H, d of d, *J* 9 and 2 Hz, 2-H), and 7.10 (1 H, d, *J* 9 Hz, 1-H); m.s. *m/e* 429 ($M^+$) (Found: C, 72.95; H, 9.0. $C_{26}H_{39}NO_4$ requires C, 72.7; H, 9.15%).

11β-(2-N,N-*Diethylaminoethyloxy*)-3-*hydroxyestra*-1,3,5-(10)-*trien*-17-*one* (10b).—A solution of the acetal (9b) (1.9 g) in acetic acid (30 ml), tetrahydrofuran (10 ml), and water (10 ml) was heated at 75 °C for 3 h. Solvent was removed under reduced pressure under nitrogen at 55 °C, and the residue cooled to 0 °C and cautiously diluted with 4% sodium hydrogen carbonate solution. The mixture was extracted with dichloromethane and the organic extracts dried ($Na_2SO_4$), filtered, and concentrated *in vacuo* to give the *ketone* (10b) (1.5 g) as a foam. Preparative t.l.c. (chloroform–methanol, 1 : 1) and subsequent crystallization from ether gave an analytical sample, m.p. 104.5—106.5 °C; $\nu_{max.}$ 3 400, 1 738, 1 610, and 1 502 cm$^{-1}$; δ 0.86 [6 H, t, *J* 8 Hz, N(CH$_2$-*Me*)$_2$], 1.09 (3 H, s, 13-Me), 2.43 [4 H, q, *J* 8 Hz, N(C*H*$_2$Me)$_2$], 3.61 br (1 H, m, 11β-OC*H*$_2$CH$_2$NEt$_2$), 4.29 (1 H, m, 11α-H), 6.48 (1 H, s, 4-H), 6.51 (1 H, d of d, *J* 9 and 2 Hz, 2-H), and 7.07 (1 H, d, *J* 9 Hz, 1-H); m.s .*m/e* 385 ($M^+$) (Found: C, 74.85; H, 8.8. $C_{24}H_{35}NO_3$ requires C, 74.75; H, 9.15%).

11β-(2-N,N-*Diethylaminoethyloxy*)-17α-*ethynylestra*-1,3,5-(10)-*triene*-3,17β-*diol* (11b).—A mixture of the ketone (10b) (0.9 g) and lithium acetylide–ethylenediamine complex (1.08 g) in dimethyl sulphoxide (27 ml) was stirred under nitrogen for 2.5 h. Additional complex (0.75 g total) was added over 1 h and the mixture stirred for an additional 1 h. The mixture was diluted with ice–water (200 ml), brought to pH 7.2 by cautious addition of acetic acid, and extracted with dichloromethane. The organic extracts were washed with water, dried ($Na_2SO_4$), filtered, and concentrated *in vacuo* to give the crude product (11b) (0.81 g) as a tan foam. The i.r. spectrum showed a very weak ketonic carbonyl

absorption. The crude product was dissolved in 95% ethanol (25 ml), and acetic acid (2.5 ml) and Girard ' P ' reagent (2.0 g) were added. The mixture was refluxed for 1 h and then concentrated *in vacuo* under nitrogen. The residue was dissolved in water, the solution brought to pH 7.2 by careful addition of saturated sodium hydrogen carbonate solution, and the mixture extracted with dichloromethane. The organic extract was dried ($Na_2SO_4$), filtered, and concentrated *in vacuo* to give the crude product (11b) (0.56 g, 58% yield) as a foam. The pure *alcohol* (11b) (0.24 g, 25% yield) was obtained by repeated crystallization from ethyl acetate, m.p. (*in vacuo*) 181.5—183.5 °C (decomp.); $\nu_{max.}$ 3 370, 3 300, 1 610, and 1 500 $cm^{-1}$; δ([$^2H_5$]pyridine) 0.88 [6 H, t, *J* 8 Hz, $N(CH_2Me)_2$], 1.51 (3 H, s, 13-Me), 2.38 [4 H, q, *J* 8 Hz, $N(CH_2Me)_2$], 3.41 (1 H, s, 17α-C≡CH), 3.61br (2 H, m, 11β-$OCH_2CH_2NEt_2$), 4.41 (1 H, m, 11α-H), 7.01br (2 H, m, 2- and 4-H), and 7.38 (1 H, d, *J* 9 Hz, 1-H); m.s. *m/e* 411 ($M^+$). An analytical sample as the hemi-hydrate was prepared by crystallization from acetonitrile–ether (Found: C, 74.5; H, 8.8. $C_{26}H_{37}NO_3 \cdot 1/2H_2O$ requires C, 74.25; H, 9.1%).

3-*Benzyloxyestra*-1,3,5(10),9(11)-*tetraen*-17-*one* (5).—A mixture of the phenol (4) [5] (90.7 g) and potassium carbonate (200 g) in dry dimethylformamide (1 200 ml) was stirred under nitrogen for 20 min. Benzyl bromide (80 ml) was added and the mixture stirred until the reaction was complete (t.l.c.). Inorganic salts were filtered off and washed with ethyl acetate. The filtrate was diluted with water and extracted with ethyl acetate, the organic extracts were washed with water and saturated sodium chloride solution, dried ($Na_2SO_4$), filtered, and concentrated *in vacuo*. Remaining traces of dimethylformamide were removed by concentration under reduced pressure under nitrogen. The residue was crystallized from ethyl acetate–hexanes to give the *benzyl ether* (5) (91.8 g). Recrystallization from ethyl acetate–hexanes afforded an analytical sample, m.p. 135—136 °C; $\nu_{max.}$ 1 740 $cm^{-1}$; δ 0.91 (3 H, s, 13-Me), 5.06 (2 H, s, $CH_2$ArH), 6.16br (1 H, m, 11-H), 6.73 (1 H, s, 4-H), 6.82 (1 H, d of d, *J* 9 and 3 Hz, 2-H), 7.40 (5 H, m, $CH_2ArH$), and 7.55 (1 H, d, *J* 9 Hz, 1-H) (Found: C, 83.55; H, 7.45. $C_{25}H_{26}O_2$ requires C, 83.75; H, 7.3%).

3-*Benzyloxy*-17,17-*ethylenedioxyestra*-1,3,5(10),9(11)-*tetraene* (6).—A mixture of the ketone (5) (91.8 g), ethylene glycol (100 ml), and toluene-*p*-sulphonic acid monohydrate (1 g) in benzene (1 200 ml) was stirred at reflux for 27 h using a Dean–Stark trap and then allowed to cool to ambient temperature. The glycol layer was drained off and extracted with benzene, and the benzene layers were combined and washed with saturated sodium hydrogen carbonate solution, water, and saturated sodium chloride solution, dried ($Na_2SO_4$), filtered, and concentrated *in vacuo*. Crystallization from acetone–hexanes afforded the pure *acetal* (6) (85 g), m.p. 135—136 °C; $\nu_{max.}$ 1 630, 1 610, and 1 570 $cm^{-1}$; δ 0.87 (3 H, s, 13-Me), 3.92 (4 H, s, 17-$OCH_2CH_2O$), 5.04 (2 H, s, $CH_2$ArH), 6.16br (1 H, m, 11-H), 6.73, (1 H, s, 4-H), 6.81 (1 H, d of d, *J* 9 and 3 Hz, 2-H), 7.41 (5 H, m, $CH_2ArH$) and 7.56 (1 H, d, *J* 9 Hz, 1-H).

3-*Benzyloxy*-17,17-*ethylenedioxyestra*-1,3,5(10)-*trien*-11α-*ol* (7a).—A cold (0 °C) solution of the tetraene (6) (30 g) in tetrahydrofuran (800 ml) under nitrogen was treated with a solution of diborane in tetrahydrofuran (1M; 420 ml). The mixture was stirred at 0 °C for 5 min and then at ambient temperature for 2 h. The mixture was then cooled to 0 °C and 10% aqueous sodium hydroxide (337 ml) carefully added followed by 30% aqueous hydrogen peroxide (420 ml). The mixture was stirred at 0 °C for 5 min and then at room temperature overnight, diluted with water, and extracted with ethyl acetate. The organic phase was washed well with saturated sodium chloride solution, dried ($Na_2SO_4$), filtered, and concentrated *in vacuo*. The residue was redissolved in ethyl acetate, filtered through Celite and silica gel, and the filtrate concentrated *in vacuo*. The residue was purified by preparative h.p.l.c. on one silica cartridge with ethyl acetate–hexanes (40 : 60) to give the *alcohol* (7a) (22.1 g). An analytical sample was obtained as an oil by dry column chromatography on silica gel (ether–hexanes, 8 : 2); $\nu_{max.}$ 3 450, 1 607, 1 575, and 1 497 $cm^{-1}$; δ 0.85 (3 H, s, 13-Me), 3.92 (4 H, m, 17-$OCH_2CH_2O$), 3.94—4.33br (1 H, m, 11β-H), 5.03 (2 H, s, $CH_2ArH$), 6.76 (1 H, s, 4-H), 6.79 (1 H, d of d, *J* 9 and 2 Hz, 2-H), 7.41 (5 H, m, $CH_2ArH$), and 7.88 (1 H, d, *J* 9 Hz, 1-H); m.s. *m/e* 420 ($M^+$) (Found: C, 77.4; H, 7.55. $C_{27}H_{32}O_4$ requires C, 77.1; H, 7.65%).

3-*Benzyloxy*-11α-(2-N,N-*diethylaminoethyloxy*)-17,17-*ethylenedioxyestra*-1,3,5(10)-*triene* (8a).—The alcohol (7a) (5.0 g) in tetrahydrofuran (90 ml) was treated with sodium hydride (10 g of a 50% dispersion) in tetrahydrofuran (90 ml) and then with 2-*N*,*N*-diethylaminoethyl bromide hydrobromide (3.4 g) at 45 °C for 43 h as described previously. The crude product (7.4 g) in ethyl acetate was combined with that (2.4 g) of another batch and filtered through a short column of silica gel to give the pure *diether* (8a) (7.7 g, 90% yield) as a pale yellow oil. An analytical sample was obtained by preparative t.l.c. (chloroform–methanol, 1 : 1) $\nu_{max.}$ (film) 1 610 and 1 495 $cm^{-1}$; δ 0.83 (3 H, s, 13-Me), 1.03 [6 H, t, *J* 8 Hz, $N(CH_2Me)_2$], 2.59 [4 H, q, *J* 8 Hz, $N(CH_2Me)_2$], 3.41—3.88br (3 H, m, 11β-H and 11α-$OCH_2CH_2NEt_2$), 3.91 (4 H, m, 17-$OCH_2CH_2O$), 5.04 (2 H, s, $CH_2ArH$), 6.73 (1 H, s, 4-H), 6.77 (1 H, d of d, *J* 8 and 3 Hz, 2-H), 7.40 (5 H, m, $CH_2ArH$), and 7.69 (1 H, d, *J* 8 Hz, 1-H); m.s. *m/e* 519 ($M^+$) (Found: C, 76.0; H, 8.55. $C_{33}H_{45}NO_4$ requires C, 76.25; H, 8.75%).

11α-(2-N,N-*Diethylaminoethyloxy*)-17,17-*ethylenedioxyestra*-1,3,5(10)-*trien*-3-*ol* (9a).—Hydrogenolysis of the diether (8a) (3.0 g) with 5% palladium on carbon (3.0 g) and hydrogen (24 lb $in^{-2}$) in ethanol (100 ml) was carried out as previously described. The crude product (2.19 g) was combined with that (2.3 g) from a similar batch to give the *monoether* (9a) (2.26 g as a solid and 2.0 g as an oil) after trituration with ether. Recrystallization from ether gave an analytical sample, m.p. 87—88 °C; $\nu_{max.}$ 3 400, 1 610, 1 580, and 1 500 $cm^{-1}$; δ 0.80 (3 H, s, 13-Me), 1.06 [6 H, t, *J* 8 Hz, $N(CH_2Me)_2$], 2.71 [4 H, q, *J* 8 Hz, $N(CH_2Me)_2$], 3.40—3.90br (3 H, m, 11β-H and 11α-$OCH_2CH_2NEt_2$), 3.91 (4 H, m, 17-$OCH_2CH_2O$), 6.18br (1 H, s, 3-OH), 6.59 (2 H, m, 2- and 4-H), and 7.50 (1 H, d, *J* 9 Hz, 1-H); m.s. *m/e* 429 ($M^+$) (Found: C, 72.15; H, 9.3. $C_{26}H_{39}NO_4$ requires C, 72.7; H, 9.15%).

11α-(2-N,N-*diethylaminoethyloxy*)-3-*hydroxyestra*-1,3,5(10)-*trien*-17-*one* (10a).—Deacetalization of the acetal (9a) (4.0 g) in acetic acid (60 ml), tetrahydrofuran (20 ml), and water (20 ml) was accomplished as previously described. The crude product was treated with activated carbon in methanol to give an oil (3.6 g). Crystallization from ether gave the *ketone* (10a) (2.18 g, 60% yield) as a pale blue powder, m.p. 171—172 °C. Recrystallization from ether afforded an analytical sample, m.p. 171—172 °C; $\nu_{max.}$ 3 400, 1 740, 1 610, 1 580, and 1 500 $cm^{-1}$; δ 0.83 (3 H, s, 13-Me), 1.05 [6 H, t, *J* 8 Hz, $N(CH_2Me)_2$], 2.66 [4 H, q, *J* 8 Hz, $N(CH_2Me)_2$], 3.43—4.07br (3 H, m, 11β-H and 11α-$OCH_2CH_2NEt_2$), 6.57 (2 H, m, 2- and 4-H), and 7.47 (1 H, d,

*J* 9 Hz, 1-H); m.s. *m/e* 385 ($M^+$) (Found: C, 74.55; H, 9.45. $C_{24}H_{35}NO_3$ requires C, 74.75; H, 9.15%).

11α-(2-N,N-*Diethylaminoethyloxy*)-17α-*ethynylestra*-1,3,5-(10)-*triene*-3,17β-*diol* (11a).—The ketone (10a) (0.5 g) was treated with lithium acetylide–ethylenediamine complex (0.6 g) in dimethyl sulphoxide (15 ml) for 5.5 h. Additional complex (0.4 g) was added and the mixture stirred for 18 h. Work-up as described previously gave the crude product (0.46 g) which was combined with that (1.0 g) from a separate batch and treated with Girard ' P ' reagent (3.0 g) in ethanol (95%; 37 ml) and acetic acid (3.7 ml) as described earlier. The crude product was treated with activated carbon in methanol to give the product (11a) (0.555 g) after trituration with ether. Recrystallization from ether afforded the pure *alcohol* (11a) (0.437 g, 27% yield), m.p. 166—167 °C; $\nu_{max.}$ 3 400, 3 300, 1 610, 1 580, and 1 500 $cm^{-1}$; δ([$^2H_5$]pyridine) 0.93 [6 H, t, *J* 7 Hz, $N(CH_2\mathit{Me})_2$], 1.07 (3 H, s, 13-Me), 2.47 [4 H, q, *J* 7 Hz, $N(\mathit{CH}_2Me)_2$], 3.27 (1 H, s, 17α-C≡CH), 3.88—4.18br (3 H, m, 11β-H and 11α-$OCH_2CH_2NEt_2$), 7.01 (1 H, s, 4-H), 7.07 (1 H, d of d, *J* 8 and 3 Hz, 2-H), and 8.12 (1 H, d, *J* 8 Hz, 1-H); m.s. *m/e* 294 ($M^+ - 117$) (Found: C, 75.55; H, 8.85. $C_{26}H_{37}NO_3$ requires C, 75.85; H, 9.05%).

*Biological Activity*.—Using the earlier published protocols,[8] the new compounds (11a) and (11b) were screened for estrogenicity, anti-estrogenicity, and post-coital activity. No significant biological activity was observed.

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