The infrared spectrum showed a very strong C=C absorption band at 1640 cm.$^{-1}$. The n.m.r. spectrum (Fig. 1) showed a typical A_2B_2 splitting for the $-CH_2-$ protons at a midpoint of τ 6.39 (8), $-O-CH_3$ protons at 6.76 (6), and $=CH_2$ protons at 7.00 (2). This spectrum was run on a Varian A-60 high resolution n.m.r. spectrometer, at a frequency of 60 Mc./sec., using $Si(CH_3)_4$ as the internal standard and at a 30% concentration in CCl_4. The numbers represent τ-values as defined by Jackman.[4] Values in parentheses indicate the ratio of the integrated areas under the peaks, and are in complete agreement with the ketene acetal structure.

Ketene Di(1-methoxy-2-propyl) Acetal (I).—To 1-methoxy-2-propanol (Ucar solvent LM, 1000 g., 11.1 moles), under a nitrogen atmosphere, was added metallic sodium (100 g., 4.35 g.-atoms) to form a solution of the sodium alcoholate in the alcohol. Vinylidene chloride (300 g., 3.10 moles) was slowly added to the above solution at an initial temperature of 90°, with rapid stirring and under a nitrogen atmosphere. During the addition of the vinylidene chloride, the temperature of the reaction mixture increased from 90 to 140°, with the concomitant precipitation of solid sodium chloride. The reaction mixture was then filtered to yield a tan-colored filtrate and solid sodium chloride. The solid was washed several times with anhydrous ether and oven-dried overnight to give 235 g. (92.5% yield based on the sodium) of sodium chloride. The liquid filtrate was vacuum distilled to yield 206 g. (1.01 moles, 46.6%, b.p. 58–59° at 3.0 mm.) of ketene di(1-methoxy-2-propyl) acetal as the higher boiling product fraction; infrared spectrum: $\nu_{C=C}$ 1650 cm.$^{-1}$ (very strong).

Anal. Calcd. for $C_{10}H_{20}O_4$: C, 58.9; H, 9.9; mol. wt., 204. Found: C, 58.8; H, 10.1; mol. wt., 214 (Menzies–Wright in benzene).

Tri(2-ethoxyethyl) Orthoacetate (VII).—To 2-ethoxyethanol (Cellosolve solvent, 1000 g., 11.1 moles), under a nitrogen atmosphere, was added metallic sodium (100 g., 4.35 moles) to form a solution of the sodium alcoholate in the alcohol. Vinylidene chloride (250 g., 2.58 moles) was slowly added to the above solution at an initial temperature of 100°, with rapid stirring and under a nitrogen atmosphere. During the addition of the vinylidene chloride, the temperature of the reaction mixture increased from 100 to 160°, with the concomitant precipitation of solid sodium chloride. Filtration of this reaction mixture gave a total of 230 g. (after ether washing and drying, 91% based on the sodium) of sodium chloride. Vacuum distillation of the liquid filtrate gave tri(2-ethoxyethyl) orthoacetate (362 g., 1.23 moles, 56.6%, b.p. 98–100° at 0.5 mm.) as the higher boiling product fraction; infrared spectrum: the —OH, C=O, and $C=CH_2$ absorptions were completely absent.

Anal. Calcd. for $C_{14}H_{30}O_6$: C, 57.1; H, 10.3; mol. wt., 294. Found: C, 57.2; H, 10.3; mol. wt., 281 (Menzies–Wright in benzene).

The acid-catalyzed hydrolysis of the above orthoacetate gave the expected products, as shown by a vapor phase chromatogram of the distilled product mixture.

Compound	Theor. wt. in product mixture, %	Obsd. v.p.c. area in mixture, %
2-Ethoxyethanol	57.7	60.8
2-Ethoxyethyl acetate	42.3	39.2

Tri(1-methoxy-2-propyl) Orthoacetate (VI).—Ketene di(1-methoxy-2-propyl) acetal (I, 51.0 g., 0.25 mole) and 1-methoxy-2-propanol (22.5 g., 0.25 mole) were placed in a stoppered 250-ml. erlenmeyer flask. Two drops of 85% phosphoric acid were then added to the above solution, whereupon the temperature of the contents rose from about 20 to over 70°. The tightly stoppered flask was then kept at room temperature overnight. Two small pellets of potassium hydroxide were added and the mixture was vacuum distilled to yield tri(1-methoxy-2-propyl) orthoacetate as the major product fraction (54 g., 0.184 mole, 74%, b.p. 78–80° at 0.25 mm.); infrared spectrum: the —OH, C=O, and $C=CH_2$ absorptions were completely absent.

Anal. Calcd. for $C_{14}H_{30}O_6$: C, 57.1; H, 10.3; mol. wt., 294. Found: C, 56.9; H, 10.3; mol. wt., 290 (Menzies–Wright in benzene).

(4) S. L. M. Jackman, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959.

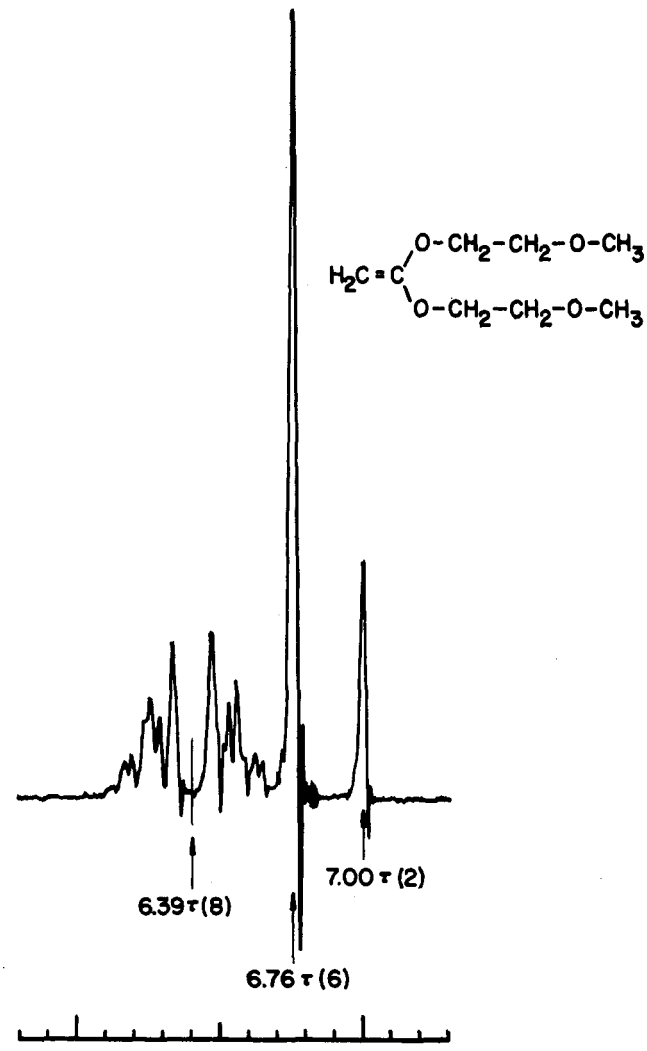

Fig. 1.—N.m.r. spectrum of ketene di(2-methoxyethyl) acetal (IV).

Acknowledgment.—It is a pleasure to acknowledge the laboratory assistance of L. J. Ford, and the analytical services of Johanna Holm, H. L. Thornburg, and R. A. Thursack.

The Synthesis of Certain 16α-Substituted Derivatives of the 3-Methyl Ethers of 16β-Cyanoestrone and 16β-Cyanoestradiol

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The possibility that modified estrogen-type compounds might be useful hypocholesterolemic agents has received considerable research attention in recent years.[1] In particular, mono- and disubstitution at the 16-position of estrone, estradiol, and their 3-etherified derivatives has been reported to give com-

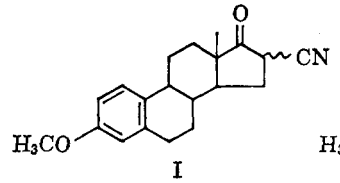
(1) See V. A. Drill and B. Riegel, *Recent Progr. Hormone Res.*, **14**, 50 (1958), for a brief resume of the rationale to this approach.

pounds of interest in this direction.[1-3] Therefore, the observation[4] in our laboratories that 16-cyanoestrone 3-methyl ether (I) and 16-cyanoestradiol 3-methyl ether[5] showed apparently enhanced hypocholesterolemic/uterotropic ratios when compared with those of the parent estrone and estradiol 3-methyl ethers prompted us to prepare certain 16-substituted derivatives of these lead compounds.

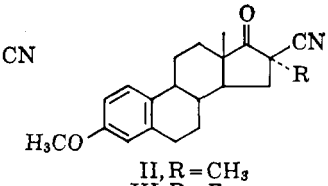
We have previously reported these compounds without specifying the configuration of the cyano substituent. It should now be noted that n.m.r. data (two C-18 methyl signals at τ 8.95 and 9.03 with total intensity equal to three protons) indicates that 16-cyanoestrone 3-methyl ether (I), at least in deuteriochloroform solution, consists of two components in a 2:1 ratio. Since the ultraviolet absorption spectrum in chloroform indicates no appreciable enol content, it is presumed that these components are the two C-16 epimers.[6] Each of the two C-18 methyl signals is observed at a position which represents a shift downfield from that (τ 9.13) noted for the C-18 methyl signal in the parent compound, estrone 3-methyl ether. The major component shows the greater shift (τ 0.18) and it is therefore assigned the *cis* (18-methyl:-16-cyano) 16β-configuration,[9] this assignment being consistent with several previous observations[10] concerning epimeric stability at the 16-position of 17-keto steroids. The shift of the C-18 methyl position manifested in the presumed 16α-epimer is about τ 0.10.

The desired 16-substituted 16-cyano derivatives were obtained readily by treating the enolate anion derived from β-ketonitrile I with appropriate reagents. Thus, the 16α-methyl, fluoro, and methylthio derivatives (II–IV) of 16β-cyanoestrone 3-methyl ether were prepared by reaction with methyl iodide, perchloryl fluoride, and methanesulfenyl chloride,[12] respectively. The methylsulfinyl and methylsulfonyl derivatives V and VI were obtained by stepwise oxidation[13] with monoperphthalic acid of the methylthio derivative IV. These products were assigned the 16β-cyano structure on the basis that the usual course of reaction at C-16 proceeds *via* an attack at the α-face.[14] That at least the fluoro derivative III does in fact have the 16β-cyano-16α-fluoro structure is evidenced by the n.m.r. spectrum which shows an intact C-18 methyl signal. Recent work by Cross and Landis[15] indicates that the presence of a 16β-fluorine atom will result in the splitting of the C-18 methyl resonance.[16]

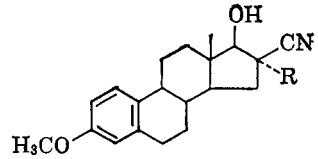
Ketonic reduction with metal borohydride of the methyl and methylthio derivatives furnished the corresponding 17-ols (VII and VIII), which are assigned the β-position by analogy.[20] Thus, metal hydride reduction of various 16β-substituted 17-ketones has been reported to give the 17β-ol without evidence of 17α-ol formation.[10c,14b,d,21-24] With 16α-substituted 17-ketones, the 17β-ol is the major product, but some 17α-ol is often noted.[14d,21,22] Therefore, in view of the good yields (70–75%) obtained for VII and VIII, our presumption seems quite reasonable.[25]



I



II, R = CH_3
III, R = F
IV, R = SCH_3
V, R = $SOCH_3$
VI, R = SO_2CH_3



VII, R = CH_3
VIII, R = SCH_3

The compounds described in this report did not show any biological advantage over the original lead compounds.[4]

(2) G. P. Mueller, W. F. Johns, D. L. Cook, and R. A. Edgren, *J. Am. Chem. Soc.*, **80**, 1769 (1958).

(3) C. H. Robinson, N. F. Bruce, and E. P. Oliveto, *J. Org. Chem.*, **28**, 975 (1963).

(4) W. Cekleniak, S. Gordon, and S. Mauer of these laboratories, private communication.

(5) H. M. Kissman, A. S. Hoffman, and M. J. Weiss, *J. Org. Chem.*, **27**, 3168 (1962).

(6) 16-Nitro 17-ketones also give an epimeric mixture (*ca.* 1:1) in deuteriochloroform.[7,8] The observed positions of the C-18 methyl signals in the 16-nitroestrone 3-methyl ether epimeric mixture represent downfield shifts of 13 and 6 c.p.s.[8]

(7) A. Hassner and J. Larkin, *J. Am. Chem. Soc.*, **85**, 2181 (1963).

(8) R. E. Schaub, W. Fulmor, and M. J. Weiss, *Tetrahedron*, **20**, 373 (1964).

(9) A downfield shift of τ 0.28 for the C-19 methyl signal has been noted for a 6β-cyano derivative [J. Jacquesy, J. Lehn, and J. Levisalles, *Bull. soc. chim. France*, 2444 (1961)].

(10) (a) A. Bowers, P. G. Holton, E. Necoechea, and F. A. Kincl, *J. Chem. Soc.*, 4057 (1961); J. H. Fried, A. N. Nutile, G. E. Arth, and L. H. Sarett, *J. Org. Chem.*, **27**, 682 (1962), 16-methyl; (b) J. Fishman and W. R. Biggerstaff, *ibid.*, **23**, 1190 (1958); G. P. Mueller and W. F. Johns, *ibid.*, **26**, 2403 (1961), 16-halo; (c) G. R. Allen, Jr., and M. J. Weiss, *ibid.*, **27**, 4681 (1962), 16-benzoyloxy; (d) 16-acetoxyepiandrosterone acetate[11] gives an approximately 1:1 epimeric mixture on equilibration.

(11) W. S. Johnson, B. Gastambide, and R. Pappo, *J. Am. Chem. Soc.*, **79**, 1991 (1957).

(12) Based on a procedure developed by H. M. Kissman and M. J. Weiss, to be published.

(13) R. E. Schaub and M. J. Weiss, *J. Org. Chem.*, **27**, 2221 (1962).

(14) Examples of apparent α-attack at C-16 in the androstane and estrane series are as follows: (a) reaction of methyl magnesium iodide with a 16-keto 17β-ol and catalytic reduction of a 16-methylene 17β-ol, H. Mori and K. Yasuda, *Yakugaku Zasshi*, **80**, 327, 330 (1960); *Chem. Abstr.*, **54**, 18,586, 18,587 (1960); (b) catalytic reduction of a 16-methylene 17-ketone, F. A. Kincl and M. Garcia, *Chem. Ber.*, **92**, 595 (1959); (c) diborane reaction with a Δ^{16}-17-acetoxy enol acetate, F. S. Alvarez and M. Arreguin, *Chem. Ind.* (London), 720 (1960); (d) halogenation of a Δ^{16}-17-acetoxy enol acetate, G. P. Mueller and W. F. Johns, *J. Org. Chem.*, **26**, 2403 (1961); (e) perchloryl fluoride reaction with a Δ^{16}-17-acetamide enamide, S. Nakanishi and E. V. Jensen, *ibid.*, **27**, 702 (1962); (f) sodium borohydride reduction of a 16-keto 17β-ol, R. M. Dodson and S. Mizuba, *ibid.*, **27**, 698 (1962).

(15) A. D. Cross and P. W. Landis, *J. Am. Chem. Soc.*, **84**, 3784 (1962).

(16) We take this occasion to note that our previously reported[17] 16-fluoro derivative of testosterone is most probably the 16β-*isomer*. The physical constants for this substance are in good agreement with the product originally described[18] as the 16α-epimer but which apparently has since been established as the 16β-epimer.[19] This conclusion is supported by the n.m.r. spectrum of our product which shows a splitting (doublet centered at 52 c.p.s., J = 1 c.p.s.; Varian A-60, tetramethylsilane internal standard, in deuteriochloroform) of the C-18 methyl resonance.

(17) H. M. Kissman, A. S. Hoffman, and M. J. Weiss, *J. Org. Chem.*, **26**, 973 (1961).

(18) J. Fried and G. H. Thomas, U. S. Patent 2,857,403 (1958).

(19) J. Fried, see ref. 14e, footnote 7.

(20) Relative to the parent 16-unsubstituted derivatives, compounds II, III, IV, VII, and VIII show a shift downfield for the C-18 methyl signal of τ 0.16–0.21 (deuteriochloroform).

(21) W. R. Biggerstaff and T. F. Gallagher, *J. Org. Chem.*, **22**, 1220 (1957).

(22) J. Fishman and W. R. Biggerstaff, *ibid.*, **23**, 1190 (1958).

(23) B. Ellis, D. Patel, and V. Petrow, *J. Chem. Soc.*, 800 (1958).

(24) A. Bowers, P. G. Holton, E. Necoechea, and F. A. Kincl, *ibid.*, 4057 (1961).

(25) However, it should be noted that most of the cited examples involved the use of lithium aluminum hydride, whereas our reductions were effected with lithium borohydride in tetrahydrofuran for VII and with sodium borohydride in ethanol for VIII.

Experimental

General.—Melting points were taken in an open capillary tube and are corrected. The ultraviolet spectra were determined in methanol on a Cary recording spectrophotometer and infrared spectra (pressed potassium bromide disks) were carried out with a Perkin-Elmer spectrophotometer (Model 21). N.m.r. data were determined with tetramethylsilane as an internal standard in deuteriochloroform with a Varian Model DP-60 spectrometer at 56.4 Mc. All evaporations were carried out under reduced pressure, and the petroleum ether used was that fraction boiling at 60–70°. Nitrogen analyses were by the Dumas method.

16β-Cyano-3-methoxy-16α-methylestra-1,3,5(10)-trien-17-one (II).—To a solution of 500 mg. of 16-cyano-3-methoxyestra-1,3,5(10)-trien-17-one[5] (I) in 25 ml. of reagent acetone, through which nitrogen was bubbled, was added 1 g. of anhydrous potassium carbonate and 2 ml. of methyl iodide. The mixture was allowed to stir under a nitrogen atmosphere for 2 days after which time another 2 ml. of methyl iodide was added and stirring was continued for an additional 5 days. The mixture then was filtered and the mother liquor was evaporated to dryness. The residue was recrystallized from acetone–water to give 442 mg. (85%) of product, m.p. 173–176°. Recrystallization from acetone–petroleum ether and then from ether–petroleum ether gave white crystals, m.p. 185–186°; $[\alpha]^{25}D$ +108° (*c* 0.58, $CHCl_3$); λ_{max} 221 mμ (ε 9400), 279 (2100), 288 (1940); λ_{max} 4.48, 5.68, 6.18, 6.34, 6.66, 6.86, 7.96 μ; n.m.r.,[26] τ 8.90 (C-18 CH_3), 8.50 (C-16 CH_3), 6.26 (OCH_3).

Anal. Calcd. for $C_{21}H_{28}NO_2$: C, 77.98; H, 7.79; N, 4.33. Found: C, 77.77; H, 8.28; N, 4.22.

16β-Cyano-16α-fluoro-3-methoxyestra-1,3,5(10)-trien-17-one (III).—Perchloryl fluoride was bubbled briskly into a cold (−4°) stirred solution of 16-cyano-3-methoxyestra-1,3,5(10)-trien-17-one[5] and 3.3 ml. of 1 *N* methanolic sodium methoxide in 20 ml. of methanol until neutral (4 min.). After flushing with nitrogen, the solution was concentrated to a small volume, diluted with water, and extracted twice with methylene chloride. The combined extracts were washed with water, dried with anhydrous magnesium sulfate, and evaporated to dryness. Recrystallization of the residue from ether–petroleum ether gave 308 mg. (58%) of product, m.p. 153–155°. Recrystallization from the same solvent pair furnished white crystals, m.p. 154–155°; $[\alpha]^{25}D$ +185° (*c* 1.1, $CHCl_3$); λ_{max} 222 mμ (ε 9000), 279 (1960), 288 (1960); λ_{max} 4.45, 5.63, 6.19, 6.34, 6.65, 7.98 μ; n.m.r.,[26] τ 8.90 (C-18 CH_3), 6.25 (OCH_3).

Anal. Calcd. for $C_{20}H_{22}FNO_2$: C, 73.37; H, 6.77; F, 5.80; N, 4.28. Found: C, 73.09; H, 6.90; F, 5.63; N, 4.40.

16β-Cyano-3-methoxy-16α-methylthioestra-1,3,5(10)-trien-17-one (IV).[12]—16-Cyano-3-methoxyestra-1,3,5(10)-trien-17-one (1.54 g., 5 mmoles) was dissoved in 20 ml. of methanol and 5 ml. of a 1 *N* methanolic sodium methoxide solution. The yellow solution was evaporated at 40° and the residue was evaporated with 10 ml. of dry dioxane to remove traces of methanol. The residue was mixed with 30 ml. of dioxane and to the yellow suspension was added 470 mg. (theory, 450 mg.) of methanesulfenyl chloride.[27] Most of the solid went into solution within a few minutes and the faintly yellow solution was evaporated at 40°. The residue was dissolved in benzene and the solution was washed with water till neutral and then dried, decolorized, and evaporated. The residue was crystallized from ether to afford 755 mg., m.p. 113–115°; $[\alpha]^{25}D$ +115° (*c* 1.05, $CHCl_3$); λ_{max} 225 mμ (ε 7453), 278 (2134), 288 (1952); λ_{max} 4.44, 5.73 μ; n.m.r.,[28] τ 8.95 (C-18 CH_3), 7.59 (S–CH_3), 6.25 (OCH_3).

Anal. Calcd. for $C_{21}H_{25}NO_2S \cdot 0.1H_2O$: C, 70.57; H, 7.11; N, 3.92; S, 8.93; H_2O, 0.5. Found: C, 70.46; H, 6.93; N, 4.15 (Kjeldahl); S, 9.23; H_2O, 0.5.

16β-Cyano-3-methoxy-16α-methylsulfinylestra-1,3,5(10)-trien-17-one (V).—To a solution of 300 mg. of 16β-cyano-3-methoxy-16α-methylthioestra-1,3,5(10)-trien-17-one (IV) in 7.5 ml. of methylene chloride was added 1.05 mole equivalents of ethereal monoperphthalic acid. The reaction mixture, protected from moisture, was allowed to stand at room temperature for 24 hr. during which period phthalic acid separated. The phthalic acid was filtered and the filtrate was washed with dilute sodium carbonate solution and water, dried with anhydrous magnesium sulfate, and evaporated to dryness. Trituration of the residue with petroleum ether and filtration afforded 254 mg. (81%) of product, m.p. 148–150° (gas). Recrystallization from methylene chloride–ether gave white crystals, m.p. 149–151° (gas); $[\alpha]^{25}D$ +125° (*c* 0.97, $CHCl_3$); λ_{max} 221 mμ (ε 10,800), 279 (2040), 288 (2040); λ_{max} 4.48, 5.71, 6.18, 6.34, 6.65, 7.96, 9.22 μ.

Anal. Calcd. for $C_{21}H_{25}NO_3S$: C, 67.89; H, 6.78; N, 3.77; S, 8.63. Found: C, 67.16; H, 6.86; N, 3.78; S, 8.92.

16β-Cyano-3-methoxy-16α-methylsulfonylestra-1,3,5(10)-trien-17-one (VI).—16β-Cyano-3-methoxy-16α-methylsulfinylestra-1,3,5(10)-trien-17-one (V, 110 mg.) was treated with monoperphthalic acid according to the procedure described above for the sulfoxide (V) preparation, except that the time was extended to 48 hr. Evaporation of methylene chloride solvent gave a semisolid which was recrystallized twice from acetone–petroleum ether to furnish 70 mg. (61%) of product, m.p. 164–166° (gas); λ_{max} 222 mμ (ε 4300), 279 (2130), 288 (2130); λ_{max} 4.46, 5.67, 6.18, 6.33, 6.65, 7.50, 7.98, 8.49 μ.

Anal. Calcd. for $C_{21}H_{25}NO_4S$: C, 65.09; H, 6.50; N, 3.61; S, 8.27. Found: C, 64.91; H, 6.58; N, 3.29; S, 8.06.

16β-Cyano-17β-hydroxy-3-methoxy-16α-methylestra-1,3,5(10)-triene (VII).—Treatment of 200 mg. of 16β-cyano-3-methoxy-16α-methylestra-1,3,5(10)-trien-17-one (II) in 20 ml. of purified tetrahydrofuran with 100 mg. of lithium borohydride for 3 hr. according to the procedure described below for the preparation of 16β-cyano-17β-hydroxy-3-methoxy-16α-methylthioestra-1,3,5-(10)-triene (VIII) afforded 150 mg. (75%) of product, m.p. 205–207°. Recrystallization from methylene chloride–ether gave white crystals, m.p. 208–210°; $[\alpha]^{25}D$ +51.5° (*c* 0.53, $CHCl_3$); λ_{max} 220 mμ (ε 8000), 279 (1870), 288 (1790); λ_{max} 2.90, 4.96, 6.19, 6.34, 6.66, 7.97 μ; n.m.r.,[28] τ 9.05 (C-18 CH_3), 8.48 (C-16 CH_3), 6.29 (OCH_3).

Anal. Calcd. for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.55; H, 8.10; N, 4.29.

16β-Cyano-17β-hydroxy-3-methoxy-16α-methylthioestra-1,3,5(10)-triene (VIII).—To a solution containing 200 mg. of 16β-cyano-3-methoxy-16α-methylthioestra-1,3,5(10)-trien-17-one (IV) in 20 ml. of absolute ethanol was added 200 mg. of sodium borohydride and the resulting suspension was stirred at room temperature for 1 hr. Acetic acid was added carefully, followed by water. The resulting solution was evaporated to near dryness and the wet residue was extracted twice with methylene chloride. The combined extracts were washed with water, dried with anhydrous magnesium sulfate, and evaporated to dryness. Recrystallization of the residue from ether–petroleum ether furnished 140 mg. (70%) of product, m.p. 185–190°. Recrystallization from methylene chloride–ether–petroleum ether gave white crystals, m.p. 190–193°; $[\alpha]^{25}D$ +59° (*c* 0.29, $CHCl_3$); λ_{max} 220 mμ (ε 8600), 279 (1960), 288 (1880); λ_{max} 2.90, 4.46, 6.18, 6.38, 6.66, 7.98 μ; n.m.r.,[8] τ 9.05 (C-18 CH_3), 7.64 (SCH_3), 6.25 (OCH_3).

Anal. Calcd. for $C_{21}H_{27}NO_2S$: C, 70.55; H, 7.61; N, 3.91; S, 8.97. Found: C, 70.83; H, 7.92; N, 3.88; S, 8.63.

Acknowledgment.—We wish to thank Dr. S. Gordon, Mr. W. Cekleniak, and Dr. S. Mauer for the biological assay information; Mr. L. Brancone and staff for the microanalyses; Mr. W. Fulmor and staff for the spectroscopic and polarimetric data; Dr. J. Lancaster of the Stamford Laboratories of American Cyanamid Company for the DP-60 n.m.r. data; and Dr. J. Fedrick and staff of the Preparations Laboratory for an ample supply of 16-cyanoestrone 3-methyl ether.

(26) N.m.r. of estrone 3-methyl ether: τ 9.11 (C-18 CH_3), 6.25 (OCH_3).
(27) I. B. Douglass, *J. Org. Chem.*, **24**, 2004 (1959).
(28) N.m.r. of estradiol 3-methyl ether: τ 9.25 (C-18 CH_3), 6.25 (OCH_3).

Synthesis of 3,5-Disubstituted Tetrahydro-4H-1,3,5-oxadiazin-4-ones

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Recently, interest has been shown in the use of tetrahydro-4H-1,3,5-oxadiazin-4-ones as imparting crease