complication of coupling with fluorine, no further analysis of the spectrum was attempted. Accordingly, we are unable to assign, at this time, a configuration to the 1-fluoro substituent in III.[13]

The secondary product IV from the fluorination reaction contained no fluorine, and elemental analysis and spectra suggested a 3-hydroxy-Δ^1 structure. Chromic acid oxidation of IV gave the Δ^1-3-ketone I. Since IV differs in physical properties from the known 17β-acetoxy-5α-androst-1-en-3β-ol,[2,14] the 3α-epimeric structure is assigned. Olefinic proton spectra already mentioned[11] and the triplet signal at 4.08 ppm (J = 4 cps) of the C-3 proton support in detail the 3α-hydroxy-Δ^1 structure of IV.[15]

In bioassay by a modified Hershberger, *et al.*, procedure,[17] the fluoro olefin III exhibited approximately 2% of the androgenic and 18% of the anabolic activity of testosterone propionate. This separation of activities for III compares favorably with data published for the nonfluorinated analog 5α-androst-2-en-17β-ol,[2] and thus constitutes further support of the concepts of A-ring sp^2 hybridization necessary for high anabolic activity.

Experimental Section[18]

5α-Androst-2-ene-1α,17β-diol (IIa).—A solution of 29 g of 17β-acetoxy-5α-androst-1-en-3-one (I) in 500 ml of methanol was cooled to 15–18° and stirred while 108 ml of 4 *N* NaOH solution and 108 ml of 30% H_2O_2 were added dropwise over 30 min. The mixture was stirred for 10 min, 100 ml of water was added, the mixture was filtered, and the product was washed successively with water and methanol and dried. The 1α,2α-epoxide (11.5 g) was dissolved in 240 ml of 2-propanol, and 60 ml of hydrazine hydrate and 3 ml of acetic acid were added. The solution was heated on a steam bath for 30 min, then held at room temperature for 1 hr. Ice and water were added, and the product was extracted with ethyl acetate. Evaporation of the extract gave an oil which was chromatographed on 450 g of alumina (activity III). Elution with benzene–$CHCl_3$ (1:1) gave 3.64 g of IIb, mp 155–155.5° after recrystallization from methanol–hexane (lit.[2] mp 158–160°); δ = 0.70 (C-19 protons), 0.77 (C-18 protons), 2.02 (17β-acetoxyl protons), 3.70 (broad, half-width 7 cps, 1β-proton), 4.59 (triplet, J = 8 cps, 17α-proton), 5.79 (C-2 vinyl proton), 5.87 ppm (C-3 vinyl proton). Continued elution of the column with the same solvent pair gave 656 mg of the 1α,17β-diol, which was recrystallized from acetone–hexane, yielding 514 mg of IIa: mp 143–144°; $[\alpha]D$ +143°; λ_{max}^{KBr} 3.03 μ etc.; δ = 0.74 (C-18 and C-19 protons), 3.4–3.8 (multiplets, 1β- and 17α-protons), 5.85 ppm (broad, 2H, C-2 and C-3 vinyl protons).

Anal. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.71; H, 10.55.

1ξ-Fluoro-5α-androst-2-en-17β-ol 17β-Acetate (III).—A solution of 3.6 g of IIb in 30 ml of CH_2Cl_2 under nitrogen was treated with 3 ml of 2-chloro-1,1,2-trifluoroethyldiethylamine. The solution was stirred at room temperature for 30 min, at which time no starting material was detected on thin layer chromatograms. Solid $NaHCO_3$ was added, the mixture was washed with water until neutral, and the CH_2Cl_2 was evaporated under vacuum. The residue was crystallized from methanol, yielding 1.9 g of product, mp 150–156°. Recrystallization from methanol gave 1.46 g of pure III: mp 156–159°; $[\alpha]D$ +102°; λ_{max}^{KBr} 5.76 8.08 μ, etc.; δ = 0.73 (doublet, J = 1.5 cps, C-19 protons), 0.80 (C-18 protons), 2.03 (17β-acetoxyl protons), 4.50 (doublet of doublets, $J_{1,2}$ = 5 cps, J_{HF} = 50 cps, 1-proton), 4.60 (triplet, J = 7 cps, 17α-proton), 5.85 (doublet, J = 5 cps, C-2 vinyl proton), 5.90 ppm (C-3 vinyl proton); in carbon tetrachloride, δ = 0.72 (doublet, J = 1.5 cps, C-19 protons), 0.78 (C-18 protons), 2.00 (17β-acetoxyl protons), 4.50 (doublet of doublets, $J_{1,2}$ = 5 cps, J_{HF} = 50 cps, 1-proton), 4.65 (triplet, J = 8 cps, 17α-proton), 5.94 ppm (broad, 2 H, C-2 and C-3 vinyl protons).

Anal. Calcd for $C_{21}H_{31}FO_2$: C, 75.41; H, 9.34; F, 5.68. Found: C, 75.64; H, 9.63; F, 5.72.

17β-Acetoxy-5α-androst-1-en-3α-ol (IV).—Reperition of the fluorination reaction with 1.12 g of IIb in 40 ml of CH_2Cl_2 and 2.8 ml of 2-chloro-1,1,2-trifluoroethyldiethylamine gave a crude crystalline product, 801 mg, which consisted mainly of the desired product, III, together with some IV. Chromatography of the material on 130 g of silica gel and successive elution with hexane, hexane–ethyl acetate, and pure ethyl acetate failed to give any III, but the nonfluorinated polar component IV, 241 mg, was eluted by ethyl acetate. Recrystallization from ethyl acetate gave 190 mg of IV:[20] mp 187–190°; $[\alpha]D$ −64.9°; λ_{max}^{KBr} 2.94, 5.85, 7.87, 8.02 μ, etc.; δ = 0.80 (C-18 and C-19 protons), 2.03 (17β-acetoxyl protons), 4.08 (triplet, J = 4 cps, 3β-proton), 4.60 (triplet, J = 8 cps, 17α-proton), 5.60 (quartet, $J_{2,3}$ = 4 cps, $J_{1,2}$ = 10 cps, C-2 vinyl proton), 6.08 ppm (doublet, J = 10 cps, C-1 vinyl proton).

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.58; H, 9.54.

17β-Acetoxy-5α-androst-1-en-3-one (I).—A solution of 50 mg of IV in 4 ml of acetone was oxidized with the Jones reagent (chromium trioxide) in the usual manner yielding 22.5 mg of crude I, mp 106–109°. Recrystallization from hexane gave pure I, mp 125–127°, $\lambda_{max}^{95\%EtOH}$ 230–232 mμ (ϵ 10,200), identical by infrared spectra and chromatographic behavior with an authentic sample.

(13) By assuming that no changes in conformation are involved in the Δ^2-steroids IIb and III, and by disregarding the 50-cps coupling between the 1-proton and the 1-fluoro group, then the doublet pattern of the 1-proton in III may be taken as an indication of a different configuration of the 1-proton from that in IIb. Thus a 1α-proton is suggested for III with a 1β-fluorine atom. This *cis* configuration between the 1-fluorine atom and the C-19 methyl group could account for the 1.5-cps splitting of the C-19 proton signal in III. The generalizations of Cross and Landis[6] leave open the question of coupling between 1α- and 1β-fluorine atoms and the C-19 protons. The 5α- and 9α-fluorine substituents do not split C-19 proton signals, but 12α- and 17α-fluorines do split C-18 proton signals.[6]

(14) R. E. Counsell, P. D. Klimstra, and F. B. Colton, *J. Org. Chem.*, **27**, 248 (1962). The specific rotation of the Syntex sample (−43.5°)[2] appears to be in error at least in sign and does not agree with Counsell, *et al.* (rotation +33.4°), or with a calculated $[\alpha]D$ value based on rotation data of other 3β-alcohols.

(15) The C-3 proton is coupled by 4 cps to the adjacent C-2 vinyl proton (whose signal also shows a 4-cps coupling together with a 10-cps coupling with the C-1 vinyl proton) and to the axial C-4 proton. The chemical shift of the C-3 proton is within the range recognized for saturated A-ring, axial 3α-alcohols in the 5α series (3.85–4.14 *ppm vs.* 3.08–3.70 ppm for epimeric equatorial 3β-alcohols[8]), and from this position and from the coupling pattern is equatorial. Thus, the 3α-hydroxyl group is axial. In contrast, other A-ring, epimeric, unsaturated 3-alcohols have C-3 proton spectra: a Δ^1-3α-alcohol at 4.03 ppm, a Δ^4-3β-alcohol at 4.20 ppm,[8] a $\Delta^{5(10)}$-3α-alcohol at 3.77 ppm, and a $\Delta^{5(10)}$-3β-alcohol at 4.00 ppm.[16]

(16) S. G. Levine, N. H. Eudy, and E. C. Farthing, *Tetrahedron Letters*, **No. 23**, 1517 (1963).

(17) (a) L. G. Hershberger, E. G. Shipley, and R. K. Meyer, *Proc. Soc. Exptl. Biol. Med.*, **83**, 175 (1953); (b) R. A. Edgren, *Acta Endocrinol.*, **44**, *Suppl.* **87**, 1 (1963).

(18) All melting points were taken on a Kofler block under microscopic magnification. Optical rotations were obtained on 1% solutions in chloroform. All reactions and purifications were monitored by thin layer chromatography using silica gel–rice starch chromatoplates[19] irrigated with hexane–ethyl acetate (4:1) and visualized with an acidified 10% alcoholic phosphomolybdic acid solution. Nmr spectra were obtained on 10% deuteriochloroform solutions using a Varian Associates Model A-60 spectrometer. Chemical shifts (δ) were measured downfield from an internal reference of tetramethylsilane.

(19) L. L. Smith and C. Foell, *J. Chromatog.*, **9**, 339 (1962).

(20) The 3α-alcohol IV is mentioned without physical constants: A. D. Cross and A. Bowers, U. S. Patent 3,127,429 (March 31, 1964).

Derivatives of 1- and 2-Tetralones

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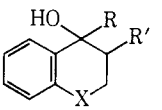
Received July 20, 1966

The preparation of intermediates related to 1- and 2-tetralones for use in the total synthesis of steroids is well documented.[1] Our interest in these intermediates

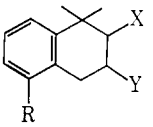
(1) L. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, pp 181–538.

TABLE I



No.	R	R′	X	Bp (mm) or mp, °C	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
1	CH=CH$_2$	H	O	76–78 (0.4)	$C_{11}H_{12}O_2$	75.06	6.87	74.93	6.69
2	C≡CH	H	O	93 (0.8)	$C_{11}H_{10}O_2$	75.93	5.79	76.17	5.98
3	C≡C—Cl	H	O	98–100 (0.3)	$C_{11}H_9ClO_2$	63.36	4.38	63.68	4.55
4	CH=CH$_2$	C_6H_5	CH_2	90	$C_{18}H_{18}O$	86.47	7.26	86.69	7.15
5	C≡CH	C_6H_5	CH_2	120–122	$C_{18}H_{16}O$	87.17	6.50	86.93	6.51
6	CH=CH$_2$	C_5H_4N(3)	CH_2	194–196	$C_{17}H_{17}NO$	81.34	6.83	81.31	6.91

TABLE II



No.	X	Y	R	Mp, °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
7	=NNHCSNH$_2$	H	H	193–194	$C_{13}H_{17}N_3S$	63.21	6.94	17.01	62.90	7.11	16.96
8	=NNHCSNH$_2$	H	OCH_3	161–163	$C_{14}H_{19}N_3OS$	60.70	6.91	15.17	60.91	6.97	14.81
9	OH	H	OCH_3	110–112	$C_{13}H_{18}O_2$	75.79	8.81		75.72	8.78	
10	$OCONH_2$	H	OCH_3	136–138	$C_{14}H_{19}NO_3$	67.53	7.69	5.63	67.87	7.61	5.45
11	=O	CHO	H	45–47	$C_{13}H_{14}O_2$	77.29	6.99		76.98	7.57	
12	=O	$CH_2N(CH_3)_2$	H	150	$C_{15}H_{21}NO\cdot HCl$	67.47	8.31	5.25	67.32	8.30	5.24
13	$OCOCH_3$	$CH_2N(CH_3)_2$	H	233–234	$C_{17}H_{25}NO_2\cdot HCl$	65.65	8.43	4.50	65.76	8.41	4.62
14	=O		H	178–180 dec	$C_{23}H_{28}N_2O\cdot HCl$	71.75	7.29	7.02	71.45	7.59	7.28

was largely influenced by their versatility as points of departure in drug synthesis. An earlier report from our laboratory had already demonstrated that 1-tetralone and 4-chromanone were useful in the synthesis of highly potent analgetics.[2] In addition, our studies with 2-phenyl-1-tetralone and 3-phenyl-4-chromanone also revealed that these substances could be transformed to 1,2-diaryl-1,2,3,4-tetrahydronaphthalines[3] and 3,4-diphenylchromanes[4] which were most active as implantation inhibitors in experimental animals. These investigations thus prompted us to explore further other modifications of these cyclic ketones. In all cases groups which are known to be responsible for particular biological effects in other systems were introduced into the molecule.

1-Tetralone and 4-Chromanone.—The compounds that were prepared in these categories are listed in Table I. Their mode of synthesis involves condensation of the appropriate Grignard or organolithium reagent with the cyclic ketone. Since our earlier studies and those of others[5] indicated these ketones were useful in the development of antifertility compounds, it seemed appropriate to prepare their 1-vinyl and 1-ethynyl derivatives. The substances outlined in Table I were not only tested for their antifertility effects but also evaluated for general pharmacological properties. They were found to be devoid of significant biological activity.

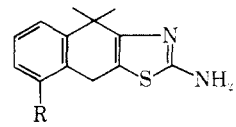
It appears from nmr considerations that a *trans* diequatorial relationship exists for the phenyl and acetylene groups in compound **5** in Table I. The proton at C_2 is centered at δ 3.22 and is a doublet of doublets. The coupling constants are approximately 11.6 and 3 cps, indicative of an axial hydrogen coupled by an adjacent axial C_3 hydrogen. A strongly deshielded aromatic proton (C_8) is at δ 8.7 and has the usual appearances associated with *ortho* and *meta* couplings. It is apparent from Dreiding models that this proton is in the deshielding zone of the acetylene moiety only if the latter group is equatorial. Compound **4** with a vinyl group at C_1 causes an upfield shift of the C_8 hydrogen into the complex aromatic region (δ 7.1–7.5). The chemical shift for C_8 is probably at δ 7.45.

2-Tetralones.—It is well known that 2-tetralone has a ready propensity to exist predominantly in the tautomeric form favoring enolization toward C_1,[6] although enolization toward C_3 is also of some consequence.[7] In order to restrict reactivity to only one reactive center α to the ketone, the 1,1-dimethyl-2-tetralone derivatives were prepared according to the general method of Robinson and co-workers.[6,8] The syntheses of 5-,[8] 6-,[9] and 7-methoxy-[10] and 5,8-dimethoxy-1,1-dimethyl-2-tetralones[11] have also been recorded. In this study only 1,1-dimethyl-2-tetralone and its 5-methoxylated

(2) G. deStevens, A. Halamandaris, P. Strachan, E. Donoghue, L. Dorfman, and C. F. Huebner, *J. Med. Chem.*, **6**, 357 (1963).
(3) W. L. Bencze, R. W. J. Carney, L. I. Barsky, A. A. Renzi, L. Dorfman, and G. deStevens, *Experientia*, **21**, 261 (1965).
(4) R. W. J. Carney, W. L. Bencze, J. Wojtkunski, A. A. Renzi, L. Dorfman, and G. deStevens, *J. Med. Chem.*, **9**, 516 (1966).
(5) D. Lednicer, J. C. Babcock, P. E. Marlatt, S. C. Lyster, and G. W. Duncan, *ibid.*, **8**, 52 (1965).
(6) J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 676 (1946).
(7) S. W. Pelletier, R. L. Chappell, P. C. Parthasarathy, and H. Lewin, *J. Org. Chem.*, **31**, 1747 (1966).
(8) J. W. Cornforth, R. H. Cornforth, and R. Robinson, *J. Chem. Soc.*, 689 (1942).
(9) H. Hart, J. L. Corbin, C. R. Wagner, and C. Wu, *J. Am. Chem. Soc.*, **85**, 3269 (1963).
(10) M. D. Soffer, J. C. Cavagnol, and H. E. Gellerson, *ibid.*, **71**, 3857 (1949).
(11) T. R. Lewis, W. B. Dickinson, and S. Archer, *ibid.*, **74**, 5321 (1952.)

derivative were used as intermediates for the synthesis of compounds of potential biological interest. The variations in structure with this group were also made according to groups known to cause specific pharmacological effects. The compounds prepared are listed in Table II. They were evaluated for their cardiovascular,[12] sedative,[13] analgetic,[14] antifertility,[3] and antiinflammatory[15] effects in experimental animals but were found to be inactive.

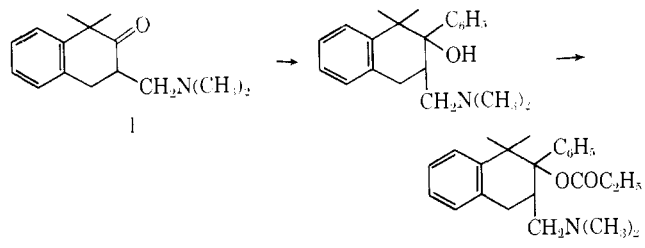
The bromination of these 2-tetralones afforded the corresponding 3-bromo ketones which readily underwent condensation with thiourea to form in good yields the desired 2-amino-4,9-dihydro-4,4-dimethylnaphtha[2,3-*d*]thiazoles (see below). These substances were also devoid of significant biological activity.



R = H, OCH_3

Finally, 1,1-dimethyl-3-dimethylaminomethyl-2-tetralone (I) was considered as a potentially useful compound for the synthesis of compounds which could elicit analgetic effects (see Scheme I). Although it was recognized from a study of Dreiding models of I that severe steric crowding around the carbonyl group would not favor Grignardization with a large group such as phenylmagnesium bromide, nevertheless, the reaction was attempted in both ether and tetrahydrofuran solvent systems. In both cases, large amounts of starting cyclic ketone were recovered. Treatment of the Mannich base with phenyllithium again afforded almost quantitative recovery of the starting material. These negative results prohibited the preparation of the desired ester of the tertiary alcohol and further work in this series was terminated.

SCHEME I



Experimental Section

All melting points were measured with a Thomas–Hoover melting point apparatus and are corrected. The boiling points are uncorrected. The nmr spectra were taken in dilute $CDCl_3$ solutions containing $(CH_3)_4Si$ as an internal standard on a Varian A-60 spectrometer. The preparation of 2-phenyl-1-tetralone and 2-(3-pyridyl)-1-tetralone have already been reported.[3]

4-Hydroxy-4-vinylchromane (1).—A solution of 40.0 g (0.41 mole) of vinyl bromide in 150 ml of dry tetrahydrofuran (THF) was added to 8.0 g (0.34 g-atom) of Mg turnings. Upon completion of this addition, a reaction had occurred with moderate reflux. The mixture was heated on the steam bath for 45 min and then chilled in an ice bath. To the reaction mixture there was then added dropwise with stirring 23.6 g (0.16 mole) of 4-chromanone dissolved in 50 ml of THF, whereupon a brisk reaction occurred. During the ketone addition the temperature of the reaction mixture was kept at 10–15°. The resulting green mixture was allowed to stand at room temperature overnight. The THF was removed by decantation and the green residue was decomposed with NH_4Cl solution (100 g of NH_4Cl in 500 ml of water). The pale yellow mixture was then extracted several times with ether and the ether extract was dried ($MgSO_4$). Removal of the drying agent by filtration yielded a light yellow extract which was evaporated to a viscous residue *in vacuo*. The oil was then distilled under high vacuum.

Compounds **4** and **6** were prepared similarly.

4-Hydroxy-4-ethynylchromane (2). A solution of 30 g (0.3 mole) of methyl bromide in 100 ml of dry ethyl ether was added slowly with good stirring to 5.0 g (0.2 g-atom) of magnesium turnings. An immediate reaction occurred in spite of the fact that the ether solution was kept at Dry Ice–acetone temperature. The addition was complete within 45 min. The resulting mixture was stirred at room temperature for 1 hr, then 150 ml of freshly distilled THF was added. Acetylene was passed through this gray mixture until the reaction temperature no longer rose above 25° (3 hr). Chromanone (14.8 g) dissolved in 50 ml of THF was added dropwise to this solution. Heat was evolved slowly and eventually a yellow mixture was formed which was stirred vigorously under N_2 for 30 min. The mixture was heated at reflux for 2 hr. After cooling to room temperature the solvent was removed by decantation. The yellow residue was decomposed with NH_4Cl solution. The mixture was extracted well with ether, and the ether extract was dried ($MgSO_4$). The $MgSO_4$ was filtered off and the ether was removed *in vacuo* to give a yellow oil which was distilled under high vacuum.

Compound **5** was also prepared in this way. This general procedure was also used on the preparation of **3**, although methyllithium was prepared and treated with *cis*-dichloroethylene to generate chloroacetylene.

A mixture of 8.7 g (0.05 mole) of 1,1-dimethyl-2-tetralone and 4.0 g (0.05 mole) of thiosemicarbazide dissolved in 100 ml of ethyl alcohol containing 1 ml of glacial acetic acid was maintained at reflux temperature on the steam bath for 3 hr. Within the first hour a copious precipitate began to form. After cooling the reaction mixture to room temperature, the white solid was collected on a Büchner funnel, washed with a small amount of ethyl alcohol, and then recrystallized from ethyl alcohol. In this way there was obtained 7.0 g of white crystals, mp 193–194°. Compound **8** was prepared by this method also.

1,1-Dimethyl-5-methoxy-2-tetralol (9).—A solution of 5.8 g (0.028 mole) of 1,1-dimethyl-5-methoxy-2-tetralone in 50 ml of ethyl ether was added dropwise to 1.1 g (0.028 mole) of $LiAlH_4$ in 75 ml of ether. An immediate reaction occurred and the reaction was carried to completion by an additional 4-hr reflux period after addition of the ketone. The mixture was then chilled to 0° and the metal hydride was decomposed by the slow addition of 10 ml of water with stirring. The mixture was allowed to come to room temperature and then filtered. The colorless filtrate was dried (Na_2SO_4). The drying agent was removed by filtration and the colorless filtrate was evaporated to dryness on the steam bath to yield a white solid. Two recrystallizations from cyclohexane yielded 4.8 g of white needles, mp 110–112°.

1,1-Dimethyl-2-tetralyl Carbamate (10).—Compound **9** (4.8 g) and 3.3 g of sodium cyanate were dissolved in 40 ml of methylene chloride and then treated with 5.7 g of trifluoroacetic acid. The color of the solution turned from pale yellow to pink and a precipitate immediately began to form. A thick precipitate was formed after 1 hr of stirring. Water (20 ml) was added to this mixture, whereupon two layers were formed. The organic layer was separated and evaporated to dryness. The resulting pink solid was recrystallized from ethyl alcohol to yield 2.6 g of white powder, mp 136–138°.

1,1-Dimethyl-3-hydroxymethylene-2-tetralone (11).—1,1-Dimethyl-2-tetralone (8.7 g, 0.05 mole) was dissolved in 100 ml toluene and the solution was chilled to 0°. Sodium hydride (6.4 g, 0.142 mole) was added portionwise with stirring under a stream of N_2. After completion of the addition, the light green mixture was stirred for 2 hr. To this mixture there was added 5.3 g (0.071 mole) of ethyl formate with stirring. A vigorous reaction immediately occurred and after 2 hr of stirring the yellow

(12) R. P. Mull, C. Tannenbaum, M. Dapero, M. Bernier, W. Yost, and G. deStevens, *J. Med. Chem.*, **8**, 332 (1965).

(13) G. deStevens, M. L. Sklar, H. Lukaszewski, and L. B. Wilkin, *ibid.*, **5**, 919 (1962).

(14) H. G. Wolff, J. D. Hardy, and H. Goodell, *J. Clin. Invest.*, **20**, 63 (1941).

(15) A. Robert and J. Nezamis, *Arch. Endocrinol.*, **25**, 105 (1957).

solid which formed was poured into an ice-cold water solution containing NH_4Cl. Two layers separated. The aqueous layer was extracted thoroughly with ether and the ether extract was dried (Na_2SO_4). The drying salt was removed by filtration and the filtrate was evaporated to dryness *in vacuo*. A yellow oil was obtained which crystallized on standing in the refrigerator. This substance was recrystallized from ethyl alcohol to afford 5.8 g of peach-colored crystals, mp 45–47°.

1,1-Dimethyl-3-dimethylaminomethyl-2-tetralone Hydrochloride (12).—A mixture of 19.6 g. (0.113 mole) of 1,1-dimethyl-2-tetralone, 9.2 g (0.128 mole) of dimethylamine hydrochloride, and 3.8 g (0.043 mole) of paraformaldehyde dissolved in 75 ml of ethyl alcohol containing 0.2 ml of concentrated HCl was heated at reflux for 8 hr. The solution was filtered from a small amount of solid material and the filtrate was evaporated to dryness *in vacuo*. The resulting white powder was recrystallized three times from ethyl alcohol to yield 7.0 g of Mannich base hydrochloride, mp 149–150°.

Compound **14** was prepared by a similar procedure.

The Mannich base **12** (6.9 g.) was dissolved in CH_3OH and 4.6 g of $NaBH_4$ was added portionwise. The solution was then heated on the steam bath for 3 hr and then evaporated to a yellow paste. The semisolid material was treated with 500 ml of an aqueous saturated NaCl solution which was in turn extracted several times with ether. The yellow ether extract was dried (Na_2SO_4). The salt was removed by filtration and the filtrate was evaporated to a light yellow oil. An infrared spectrum revealed that very little ketone was present. The acetate derivative of the carbinol, **1,1-dimethyl-3-dimethylaminomethyl-2-tetralol**, was prepared in the usual way to give 1.0 g of **13**, mp 233–234°.

2-Amino-4,9-dihydro-4,4-dimethylnaphtho[2,3-*d*]thiazole Hydrobromide.—An ether solution of 1,1-dimethyl-2-tetralone (10.0 g, 0.058 mole) was treated dropwise with stirring with 9.2 g (0.057 mole) of Br_2. The resulting pale yellow solution was evaporated to dryness *in vacuo*, the temperature being maintained below 15°, to give an orange oil which resisted all attempts to crystallize. This oil (14.5 g, 0.0586 mole) was dissolved in 100 ml of ethyl alcohol to which solution then was added 4.4 g (0.058 mole) of thiourea. The solution was heated under reflux for 3 hr. One-half of the solvent was removed *in vacuo* and the resulting solution was treated with excess ether. An oil separated from the solution This oil was triturated with acetone to give a white powder which was recrystallized from excess acetone to yield 5.2 g of product, mp 240–242°.

Anal. Calcd for $C_{13}H_{15}BrN_2S$: C, 50.20; H, 4.86; N, 9.01. Found: C, 50.24; H, 4.79; N, 8.74.

3-Bromo-1,1-dimethyl-5-methoxy-2-tetralone, mp 110–112°, was prepared as described above. It was treated directly with thiourea in ethyl alcohol to form 2-amino-4,9-dihydro-4,4-dimethyl-8-methoxynaphtho[2,3-*d*]thiazole hydrobromide, mp 276–277°.

Anal. Calcd for $C_{14}H_{17}BrN_2OS$: C, 49.31; H, 5.03; N, 8.22. Found: C, 49.57; H, 5.12; N, 7.95.

Ring-D-Bridge Steroid Analogs. IV.[1] 14α,17α-Ethenopregn-4-ene-3,20-dione[2]

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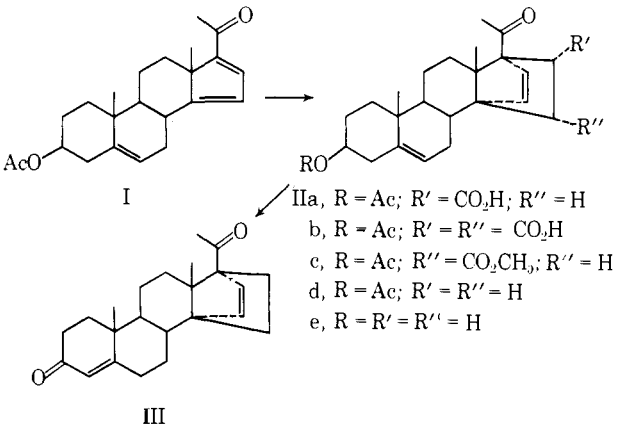
Recently[1,4,5] we have been attempting to synthesize 14α,17α-bridged analogs of steroid hormones, in order to determine the effect of such bridging on the biological activity of the hormones. Diels–Alder additions to the diene system of $\Delta^{14,16}$-steroids have afforded adducts[4,5] which are potentially suitable for transformation into progesterone analogs. The ring-D double bonds of the adducts,[5] formed by reaction of such steroidal dienes with maleic anhydride or with 4-phenyl-1,2,4-triazoline-3,5-dione, could not be reduced selectively by low-pressure catalytic hydrogenation.[6] However, such double bonds were sufficiently susceptible to intramolecular attack to prevent the oxidative decarboxylation of *endo*-carboxylic acids. Thus, an attempted Hunsdiecker reaction on IIa resulted in the formation of a halolactone,[1] and an attempted bisdecarboxylation[7] of the diacid IIb gave a complex mixture which had an infrared spectrum consistent with the presence of some of the expected[8] dilactone.

Conditions have recently been found[9] which permit the selective catalytic hydrogenation of the ring-D double bond of the acrylate adduct IIc,[4] and an attempt to degrade this reduced adduct to a simple 14α,17α-etheno- (or ethano-) bridge analog is currently being made. While the above work was in progress, a more direct approach to the desired hormone analogs was suggested by a report[10] that pressures greater than 1000 atm facilitate the addition of ethylene to dimethyl cyclohexa-1,3-diene-1,4-dicarboxylate.

Heating a benzene solution of 3β-acetoxy-20-keto-5,14,16-pregnatriene[11] (I) at 160° for 14 hr under 3000 atm of ethylene led to the formation of 14α,17α-ethenopregn-5-en-3β-ol-20-one acetate (IId) in 53% yield. The close similarity, particularly in the vinyl hydrogen region, of the nmr spectrum of IId to those of closely related Diels–Alder adducts[4,5] supports its gross structure; this evidence together with the stereospecificity of the above reaction led us to assign the stereochemistry of IIa on the basis of the same analogy.[4,5] Hydrolysis of the acetate group of IId fol-



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