(25 ml.) was treated with an ethereal monoperphthalic acid solution (0.62 *N*, 5.0 ml.). On standing at room temperature, there precipitated the crystalline 6β-hydroxy compound XVIII (0.28 g.), m.p. 272–276°. One crystallization from ethyl acetate–heptane afforded 0.145 g., m.p. 286–288°; $[\alpha]^{25}D$ +89° (chloroform); λ_{max} 232 mμ (ε 16,500); ν_{max} 3430, 1760, 1728, 1680 (shoulder), 1665, 1618, and 1060 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{35}O_6F$ (494.54): C, 63.14; H, 7.14; F, 3.84. Found: C, 63.16; H, 7.37; F, 3.51.

When the ethyl enol ether XVII[16] (1.0 g.) was oxidized as above, XVIII (0.27 g.) was also obtained, m.p. 277–280°.

9α-Fluoro-6β,11β,21-trihydroxy-16α,17α-isopropylidenedioxypregn-4-ene-3,20-dione (XIX).—Aqueous 10% potassium carbonate (1.0 ml.) was added to a suspension of 21-acetoxy-9α-fluoro-6β,11β-dihydroxy-16α,17α-isopropylidenedioxypregn-4-ene-3,20-dione (XVIII, 0.1 g.) in methanol (10 ml.) agitated by a nitrogen stream. Solution was complete in 30 min. and after an additional 15 min., the reaction mixture was neutralized with acetic acid and poured into water. The aqueous solution was extracted with ethyl acetate, and the dried extract on evaporation provided crude XIX. Crystallization from ethyl acetate–heptane yielded prisms (13 mg.), m.p. 238–241°; $[\alpha]^{25}D$ +90° (pyridine); λ_{max} 232 mμ (ε 13,600); ν_{max} 3430, 1723, 1675, (shoulder), and 1667 cm.$^{-1}$.

Anal. Calcd. for $C_{24}H_{33}O_7F$ (452.50): C, 63.70; H, 7.36; F, 4.19. Found: C, 63.83; H, 7.57; F, 3.91.

Nuclear Magnetic Resonance Spectra of Heterocyclic Compounds. II. Abnormal Products from the Ketalization of Cortisone[1]

E. CASPI, T. A. WITTSTRUCK, AND N. GROVER

Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts

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It was demonstrated that compounds having 1,2-bisethylene dioxide and *trans*-naphthodioxide moieties at C-17 are formed as ketalization by-products of steroids with a dihydroxyacetone side chain. The compounds were identified by the use of n.m.r. spectroscopy.

Protection of ketones with ethylene ketals[2] is frequently used in the synthetic elaboration of steroids.[3] Unfortunately, on many occasions and especially in the case of steroids with a dihydroxyacetone moiety the utility of the method is limited severely because the ketals are obtained in low yields, and because large amounts of unknown by-products are formed.[4]

The isolation of unidentified by-products from ketalization of dihydrocortisone,[4] cortisone, and 11-epicortisol[5] has recently been reported by two laboratories. The only product identified[5] (**12a**) was assigned its structure in analogy to **12b**, obtained by Tsuda, *et al.*,[6] as a by-product of ketalization of 17α,21-dihydroxy-4-pregnene-3,20-dione (Reichstein's substance S). To account for their observations the Japanese workers have suggested a mechanism analogous to the Mattox rearrangement.[7] Bernstein, *et al.*,[5] isolated from the mother liquors of ketalization of 11-epicortisol an 11α-hydroxy compound, $C_{27}H_{40}O_7$. They oxidized it to the 11-keto analog, $C_{27}H_{38}O_7$, m.p. 173–174°, to which we assign structure **8a** (see Fig. 2). On treatment of cortisone with anhydrous ethylene glycol containing hydrogen chloride, the Lederle group obtained another compound identified by us as **9a** (see Fig. 2).

Structures like **2**, **8**, and **10** were considered for the by-products of ketalization of corticosteroids.[4,5] Structures **8** and **10** were suggested solely on the basis of their resistance toward acid hydrolysis,[4] analogous to sugar anhydrides, sapogenins, and oxetones. Isolation[6] of **12b** and later of **12a** indicated the possible existence of compounds similar to **2**. Inspection of models revealed that the pentacyclic–heptacyclic structures **11** are also feasible. (See Flow Sheet, Fig. 2.)

It has been reported that α-dicarbonyls on treatment with ethylene glycol in the presence of acids yield *trans*-naphthodioxanes[8] and 1,2-bisdioxolanes.[9] Recent reports on the course of the Porter–Silber[10a] reaction, and on the acid-catalyzed rearrangement of the dihydroxyacetone moiety[10b] support the view that α-dicarbonyls might be formed during ketalization of steroids with such moieties, as suggested by Tsuda, *et al.*[6] Should this be the case, the unknown by-products could have 1,2-bisethylene dioxide or naphthodioxide moieties attached at C-17. Thus, in order to elucidate structures of the unknown by-products, two problems had to be solved: namely, (a) establishing the nature and points of attachment of the blocking groups in the side chain, and (b) providing conclusive proof for existence of an unchanged steroid carbon skeleton in the products. In view of the failure encountered by us (see later) and others,[4,5] in the attempted acid-catalyzed hydrolysis of the blocking groups, a chemical degradation approach was not considered promising.

In the previous paper of this series[11] we compared the n.m.r. spectra of substituted dioxolanes and dioxanes and observed the dependence of the chemical shift of the peaks for the single hydrogen on a carbon bearing two oxygens on the size of the ring. In the 2-substituted dioxolanes and 1,2-bisdioxolanes this peak appears at lower field (*ca.* τ 5.0–5.2) than does the corresponding peak for the 1,4;5,8-naphthodioxane derivative (*ca.* τ 5.3–5.5). The nature of the signals arising from the —O—CH_2—CH_2—O— moiety also appears to

(1) This work was supported by grants from U. S. Public Health Service, CY-4663 and A-5326.

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(3) R. Antonucci, S. Bernstein, R. Littell, K. J. Sax, and J. H. Williams, *J. Org. Chem.*, **17**, 1341 (1952), and other papers of this series.

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(6) K. Tsuda, N. Ikekawa, and S. Nozoe, *Chem. Pharm. Bull. Japan*, **7**, 519 (1959).

(7) V. R. Mattox, *J. Am. Chem. Soc.*, **74**, 4340 (1952).

(8) J. Boeseken, F. Tellegen, and P. C. Henriguez, *Rec. trav. chim.*, **50**, 909 (1931); J. Boeseken and F. Tellegen, *ibid.*, **57**, 133 (1958).

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(10) (a) D. H. R. Barton, T. C. McMorris, and R. Segovia, *J. Chem. Soc.*, 2027 (1961); (b) H. L. Herzog, M. Jevnik Gentles, H. Marshall, and E. B. Hershberg, *J. Am. Chem. Soc.*, **83**, 4073 (1961).

(11) E. Caspi, T. A. Wittstruck, and D. M. Piatak, *J. Org. Chem.*, **27**, 3183 (1962). Page 3189, line 22 in the reference should read 1,4;5,8-*trans*-naphthodioxane.

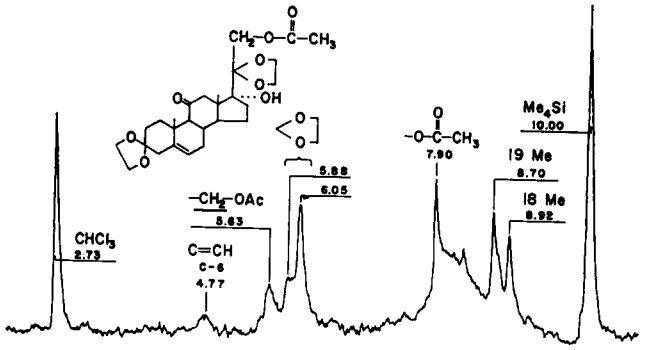

Figure 1

Flow Sheet

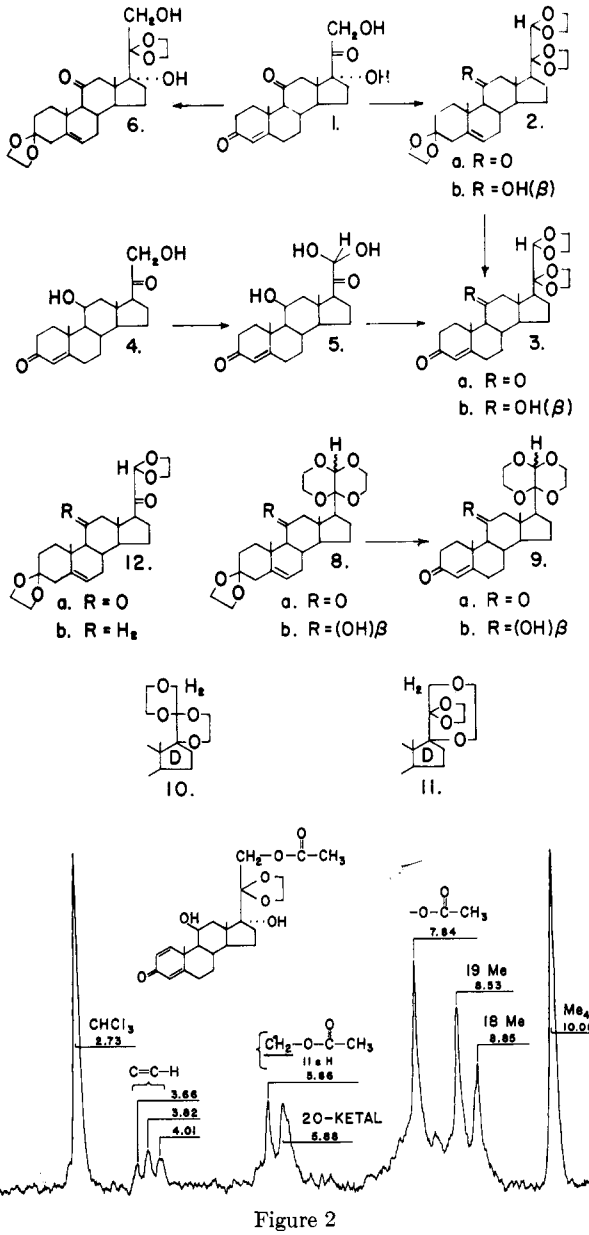

Figure 2

depend on the ring size. Unless the molecule is inverting rapidly the signal for this portion of the 1,4;5,8-naphthodioxane derivatives is distinctly split into a number of peaks, and the entire multiplet is spread over a wide range. The signal of the analogous protons in five-membered rings is generally far narrower and most often unsplit.

Based on these findings, it appeared likely that n.m.r. spectroscopy would be useful in determining the structures of the unknown by-products. To evaluate the applicability of this method to steroidal dioxolanes, the n.m.r. spectra of several steroidal mono- and diethylene dioxides were studied. The chemical shifts of the ethylene dioxide peaks are summarized in Table I. The —O—CH_2—CH_2—O— moieties gave narrow, well defined peaks,[12] although some widening and asymmetric distortion of the 20-ketal was found for cortisone-3,20-bisethylene dioxide (Fig. 1) and prednisone-20-ethylene dioxide 21-acetate (Fig. 2).

We then carried out two ketalization experiments of cortisone with ethylene glycol, and *p*-toluenesulfonic acid in the presence,[13] and in the absence,[14] of benzene. In both cases, the yield of crystalline cortisone-3,20-bis-diethylene ketal (**6**) was poor. Since the crude reaction products gave identical infrared spectra, they were combined and chromatographed on alumina. At first, a solvated mixture of products was eluted, from which **2a** was obtained after multiple crystallizations. It soon became evident that **2a** was not identical to the above cortisone-3,20-bisethylene ketal (**6**). The substance **2a**, m.p. 160–162°, had formula $C_{27}H_{38}O_7$, indicating the incorporation of three ethylene dioxide moieties and it did not absorb ultraviolet light in the 210–240-mμ region. An infrared spectrum revealed the absence of a hydroxyl group, and exhibited bands at 1700, (11-ketone), 1655 (isolated double bond), and 1055 $cm.^{-1}$. The band at 1700 $cm.^{-1}$ was tentatively assigned to the 11-ketone, because of known resistance of 11-carbonyls to ketalization under the conditions used.[5,6,8,11,15] Treatment of **2a** with aqueous acetic acid[13] gave **3a**, m.p. 150–152°, identical to the second compound eluted in 10% yield from the column. Since **3a** absorbed ultraviolet light, (238 mμ, ε 15,100), and had formula $C_{25}H_{34}O_6$, it was assumed that upon acid treatment **2a** lost the ketal moiety at C-3. Neither **2a** nor **3a** reacted with blue tetrazolium,[16] and attempts to restore the α-ketolic moiety by removing the protective groupings with boiling aqueous acetic acid or aqueous methanolic sulfuric acid, failed. Reduction with lithium aluminum hydride of the crude triketal eluted from the column gave a mixture of products from which **2b** and **8b** were isolated. When the reduced mixture of steroids was treated with aqueous acetic acid, the C-3 dioxolane group was removed and **3b** was obtained. The alcohol (**3b**) could not be acetylated with acetic anhydride–pyridine but was oxidized with chromium trioxide in pyridine to **3a**.

Initially it was considered probable that **2a** and **3a** might be identical to **8a** and **9a**, respectively. Dr. Seymour Bernstein kindly made available to us small samples of his products (**8a** and **9a**), and a comparison of the infrared spectra with those of **2a** and **3a** showed them to be distinctly different. We have then confirmed the observations of Bernstein, *et al.*,[5] on the relation of **8a** to **9a** by hydrolyzing **8a** with boiling aqueous acetic acid to yield **9a**.

(12) J. Kalvoda, G. Anner, D. Arigoni, K. Heusler, H. Immer, O. Jeger, M. Lj. Mihailovic, K. Schaffner, and A. Wettstein, *Helv. Chim. Acta*, **44**, 186 (1961).

(13) R. Antonucci, S. Bernstein, M. Heller, R. Lenhard, R. Littell, and J. H. Williams, *J. Org. Chem.*, **18**, 70 (1953).

(14) J. A. Campbell, J. C. Babcock, and J. A. Hogg, *J. Am. Chem. Soc.*, **80**, 4717 (1958).

(15) B. J. Magerlain, and R. H. Levin, *ibid.*, **77**, 1964 (1955).

(16) E. Caspi, *J. Org. Chem.*, **21**, 729 (1956).

TABLE I

CERTAIN N.M.R. BANDS OF STEROIDAL KETALS[a]

Compounds	3 ketal	20 ketal	21 ketal	17 ketal	—O—CR—O—	—OCH₂—CH₂O—	—O—C(H)—O—
Desoxycorticosterone 21-acetate, 3-ethylene ketal	6.06						
Prednisolone 21-acetate 20-ethylene ketal		5.88					
Pregnenolone 20-ethylene ketal		6.08					
Progesterone 20-ethylene ketal		6.08					
Adrenosterone 3,17-diethylene ketal	6.08			6.08			
Cortisone acetate 3,20-di-ethylene ketal	6.05	5.88					
2a	6.08	5.98	6.08		5.17		
2b		6.07	6.07		5.10		
3a		6.04	6.13		5.25		
3b		6.08	6.08		5.13		
8a	6.07					Multiplet 6.18	5.44
8b						Multiplet 6.05	5.52
9a						Multiplet 6.11	5.46

[a] Expressed in τ units.

An n.m.r. spectrum of **2a** (Fig. 3) showed bands at τ 4.71 for the C-6 proton of a Δ^5-double bond and at τ 8.79 and 9.28 for the 19 and 18 methyl groups, respectively. In addition, a band was present at τ 5.17 and two partly overlapping bands at τ 5.98 and 6.08, the latter of which was distinctly more intense. The spectrum of **3a** (Fig. 4) had bands for the C-4 proton of a Δ^4-double bond at τ 4.25 and for the 19 and 18 methyl groups at τ 8.58 and 9.21, respectively.[17] Again, a band was found at τ 5.25, and this time, the two bands at τ 6.04 and 6.13 were of approximately equal intensity. The shift of the olefinic proton from C-6, τ 4.71 to C-4, τ 4.25, taken together with the approximately 50% decrease of the intensity of the —O—CH_2—CH_2—O— band at τ 6.13, conclusively establishes the C-3 location of one of the ketals in **2a**. The bands at τ 5.17 in **2a**, and at τ 5.25 in **3a**, undoubtedly originated from single protons on carbons bearing two oxygens, and their location is in agreement with that observed for the single proton on a similar carbon in 2-substituted dioxolanes.[11] We concluded, therefore, that the two bands at τ 6.04 and 6.13 are those of the —O—CH_2—CH_2—O— moiety of two dioxolane rings. If it is assumed that the two ketals are attached to the side chain (see below), then one is undoubtedly attached at C-20. The presence of the characteristic band at τ 5.25 indicates that the second ketal must be located at C-21. The lack of coupling of the hydrogen which gives rise to the τ 5.25 band, as evidenced by the absence of band splitting indicates the absence of other protons in its vicinity, and provides additional support for attachment of the ketal group to C-21. Similarly **2b** and **3b** had bands at τ 5.12 and 5.00, respectively, for single protons in a dioxolane ring. The presence in **2** and **3** of a proton on a carbon bearing two oxygens conclusively excluded structures **10** and **11**. This exclusion was corroborated by integration of the —O—CH_2—CH_2—O—

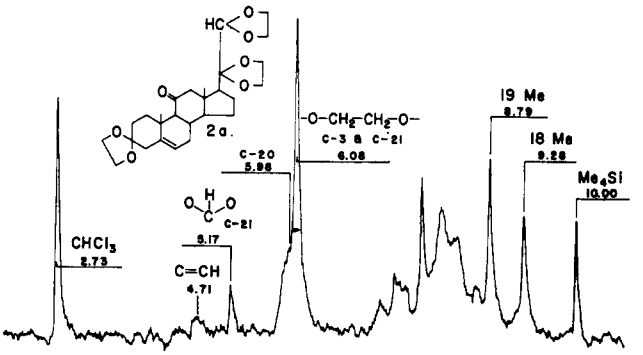

Figure 3

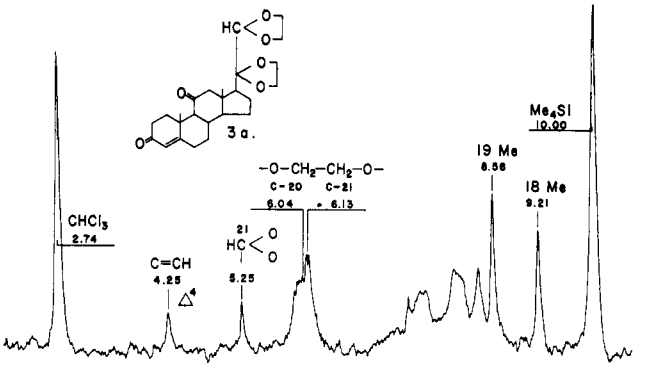

Figure 4

bands of **2a** which showed only twelve hydrogens, while structures **10** and **11** require fourteen.

An n.m.r. spectrum of **8a** (Fig. 5) exhibited bands at τ 4.67 for the C-6 proton of a Δ^5-double bond and at 8.76 and 9.16 for the 19 and 18 methyl groups, respectively. In addition, there was a band at τ 5.44 for a hydrogen on a carbon bearing two oxygens, and two overlapping bands, one a sharp band at τ 6.07 and the other a broad, distorted, multiple split band extending from τ 5.96 to about τ 6.63. Since boiling of **8a** with aqueous acetic acid gave **9a**, and since this change was accompanied by loss of the band at τ 6.07 in the n.m.r.

(17) R. F. Zürcher, *Helv. Chim. Acta*, **44**, 1380 (1961); J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958); J. S. G. Cox, E. O. Bishop, and R. E. Richards, *J. Chem. Soc.* 5118 (1960); G. Slomp and B. R. McGarvey, *J. Am. Chem. Soc.*, **81**, 2200 (1959).

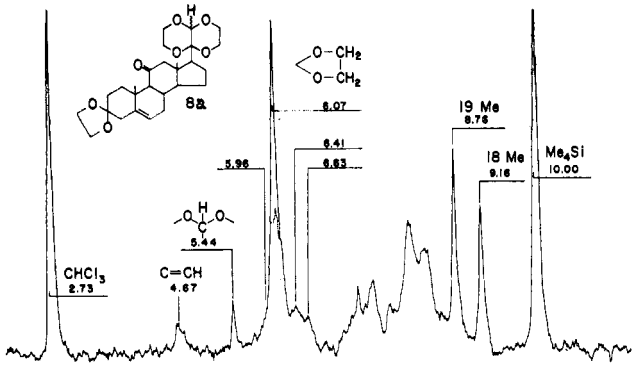

Figure 5

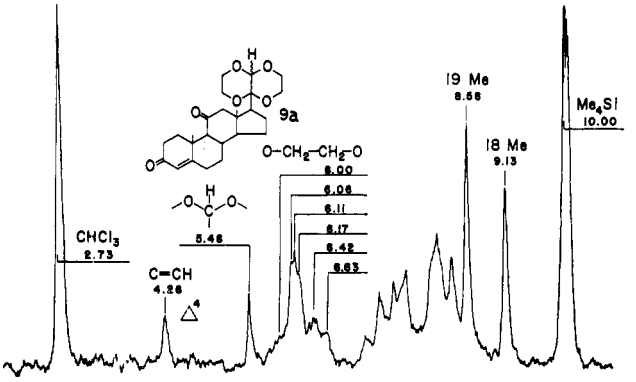

Figure 6

spectrum of **9a** (Fig. 6) and appearance of a band at τ 4.26 for the C-4 proton on a Δ^4-double bond, it is evident that the band at τ 6.07 must be ascribed to the ketal at C-3. In addition, the spectrum showed bands at τ 5.46 for a hydrogen on a carbon bearing two oxygens, and a multiple-split, distorted band ranging from about 6.00–6.63. The latter band was partially obscured in the spectrum of **8a** (Fig. 5) by the 3-ethylene ketal function. The location of the bands for single protons on a carbon bearing two oxygens in **8a** and **9a** at τ 5.44 and 5.46 differed from those observed for **2a** and **3a**. The location of these signals was in agreement[2] with the values found for 1,4;5,8-*trans*-naphthodioxane. This agreement taken together with the width of the multiple-split bands ascribable to the —O—CH_2—CH_2—O— moieties in **8a** and **9a** characteristic for 1,4;5,8-*trans*-naphthodioxane,[11] constitutes proof of the proposed structures **8a** and **9a**. Analogous results were obtained for **8b**, which showed a band at τ 5.52 for the single proton at C-21, and a broad distorted band centered at τ 6.05 for the —O—CH_2—CH_2—O— moiety. Again, the presence of bands ascribable to the single hydrogens on a carbon bearing two oxygens conclusively excluded structures **10** and **11**.

The distortion of the —O—CH_2—CH_2—O— band observed for **2**, **3**, **8**, and **9** is in contrast to the symmetry observed for the bands in dioxolanes, substituted dioxanes, and naphthodioxanes.[11] This asymmetry could possibly result from an electronic non-equivalency of the protons giving rise to these bands. Inspection of models of steroids giving distorted bands (Fig. 1–6) revealed various degrees of restriction of free rotation around the 17–20 bond. On an *average time basis*, because of the lack of complete freedom of rotation, the protons involved will not be in *equivalent electronic positions* and could produce a separation of signals.

Though the evidence presented thus far establishes the structure of **2**, **3**, **8**, and **9** experimental proof for the presence of an unchanged steroidal skeleton was lacking. To prove its presence, corticosterone (**4**) was converted to corticosterone-21-aldehyde (hydrate)[18] (**5**) which was treated with ethylene glycol and benzene in the presence of catalytic amounts of *p*-toluenesulfonic acid. Upon chromatography and fractional crystallization of the recovered steroids, **3b** and **9b** were obtained. The alcohols on oxidation gave the respective ketonic products **3a** and **9a**, establishing conclusively that **2**, **3**, **8**, and **9** are derivatives of 17-desoxycorticosterone and have an unchanged steroid skeleton.

In view of the ease with which naphthodioxanes or steroidal ketals are cleaved, the stability of the 20,21-bisethylene dioxides and 17β-*trans*-naphthodioxanes is unexplained. Possibly, the presence of two such groups on neighboring carbons exerts a stabilizing effect on the molecule.

NOTE ADDED IN PROOF.—Confirmation of structures **2** (**a**, **b**) and **3** (**a**, **b**) was obtained by an independent synthesis and will be reported (E. Caspi and H. Zajac to be published).

Experimental[19]

17α,21-Dihydroxy-5-pregnen-11-one-3,20-bisethylene Dioxide (6).—A. A mixture of cortisone (**1**), 7.5 g., ethylene glycol, 60 ml., benzene, 250 ml., and *p*-toluenesulfonic acid, 225 mg., was slowly distilled over a period of 5 hr. Then a saturated solution of sodium bicarbonate, 20 ml., was added, followed by 1000 ml. of water. The phases were separated, and the aqueous layer was extracted with ethyl acetate. The combined organic extracts were washed, dried, and concentrated to a sirup. The sirup was dissolved in methanol, and a small amount of cortisone-3,20-bisethylene dioxide (**6**) was obtained.

B. A mixture of cortisone, 10.0 g., ethylene glycol, 200 ml., and *p*-toluenesulfonic acid, 500 mg., was rapidly distilled at 100°/0.1 mm., and 100 ml. of distillate was collected. The reaction mixture was cooled to 50°, and the separated solid was collected. A total of 14.30 g. of a nonhomogeneous solid was obtained in several crops, from which 850 mg. of homogeneous **6** was isolated after multiple recrystallizations.

A sample was crystallized several times from methanol, m.p. 215–216°, λ_{max}^{MeOH} no specific absorption in the 220–240-mμ region; ν_{max}^{KBr} 3680, 3560 (shoulder), 1695, 1665 (double bond), 1105 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{36}O_7$: C, 66.94; H, 8.09. Found: C, 67.12; H, 8.23.

C. Upon chromatography of the combined noncrystalline residues from experiment A and B, 4.1 g. of **6** was obtained (see below). The product was eluted with benzene–chloroform (3:2).

5-Pregnen-11-one-3,20,21-trisethylene Dioxide (2a).—All the sirupy residues (15.5 g.) from experiments A and B were combined, and chromatographed on Woelm neutral alumina activity II. Elution of the column with benzene and mixtures of benzene and chloroform gave at first a gelatinous residue (a), then two solids **3a**, 1.6 g., and **6**, 4.1 g.

The gelatinous residue was dried for 4 hr. at 70° to yield a powder, 4.5 g. The powder on repeated crystallizations from acetone gave **2a**.

A sample of **2a** was recrystallized from acetone to a m.p. 160–162°; λ_{max}^{MeOH} no specific absorption in the 220–240-mμ region; ν_{max}^{KBr} 1700, 1665, 1055 cm.$^{-1}$. N.m.r. τ 4.71, 5.17, 5.98, 6.08, 8.79, 9.28.

Anal. Calcd. for $C_{27}H_{38}O_7$: C, 68.33; H, 8.07. Found: C, 68.31, 67.95; H, 8.05, 7.75.

(18) W. J. Leanza, J. P. Conbere, E. F. Rogers, and K. Pfister, *J. Am. Chem. Soc.*, **76**, 1691 (1954).

(19) Melting points were taken on a micro hot stage and are corrected. Ultraviolet spectra were determined on methanolic solutions on a Cary Model 11 MS or 14 spectrophotometers. The n.m.r. spectra were determined in deuterated chloroform exactly as described in ref. 11 and the results are expressed in τ units. Analyses were made by Dr. W. J. Kirsten, Uppsala, Sweden.

4-Pregnene-3,11-dione-20,21-bisethylene Dioxide (3a).—A. Elution of the column described above with benzene–chloroform (1:99 through 1:4) gave 1.6 g. of **3a**.

B. A mixture of **2a**, 50 mg., acetic acid, 4 ml., and water, 2 ml., was heated for 1 hr. on a boiling water bath. The product (**3a**) was recovered in the conventional manner.

C. A solution of **2a**, 50 mg., in methanol, 12 ml., and 2 *N* sulfuric acid, 1.5 ml., was stored for 30 min. at room temperature. The product **3a** was recovered by extraction with ether (48 mg.).

D. A mixture of **2a**, 50 mg., methanol, 12 ml., and 2 *N* sulfuric acid, 1.5 ml., was boiled for 30 min. The product **3a** was recovered with ether (50 mg.).

E. A solution of **3b**, 21.4 mg., in pyridine, 0.2 ml., was added to a suspension of chromium trioxide, 35 mg., in pyridine, 0.2 ml., and the mixture was agitated for 16 hr. at room temperature. The steroids were recovered with ethyl acetate,[20] and the product was crystallized from methanol, 8.7 mg., m.p. 150–152°.

Repeated recrystallizations from methylene chloride–methanol gave a sample, m.p. 150–152°; λ_{max}^{MeOH} 238 mμ, ε 15,100; ν_{max}^{KBr} 1710, 1665, 1610, 1215, 1065 cm.$^{-1}$. N.m.r. τ 4.25, 5.25, 6.04, 6.13, 6.17, 6.58, 9.21.

Anal. Calcd. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.62; H, 8.04.

11β-Hydroxy-5-pregnen-3,20,21-trisethylene Dioxide (2b).—The previously described powder (a), 500 mg., was dissolved in tetrahydrofuran–ether (3:1), 100 ml., then lithium aluminum hydride was added, and the suspension was boiled for 4 hr. The reaction was terminated with acetone. Then a small amount of water was added, the precipitated solid was filtered, and the filtrate was concentrated. The steroids were recovered with ethyl acetate in the conventional manner. The residue was moistened with ether–methanol to yield **8b**. The mother liquor was concentrated to a residue and crystallized from methanol to yield **2b**.

A sample of **2b** was crystallized from ethyl acetate, m.p. 102–106°. λ_{max}^{MeOH} no specific absorption in the 220–240-mμ region; ν_{max}^{KBr} 3500, 1100, 1080 cm.$^{-1}$. N.m.r. τ 4.77, 5.10, 5.4 (11α H), 6.07, 8.71, 8.93, and 8.96.

Anal. Calcd. for $C_{27}H_{40}O_7$: C, 68.04; H, 8.46. Found: C, 67.92; H, 8.23.

11β-Hydroxy-5-androsten-17β-[4α]-[1,4;5,8]-*trans*-naphthodioxane-3-ethylene Dioxide (8b).—The above described sample of **8b** was crystallized several times from methanol m.p. 168–170°; λ_{max}^{MeOH} no specific absorption in the 220–240-mμ region; ν_{max}^{KBr} 3650, 1100, 1095 cm.$^{-1}$. N.m.r. τ 4.83, 5.41, 5.52, 6.05, 8.72, 8.92.

Anal. Calcd. for $C_{27}H_{40}O_7$: C, 68.04; H, 8.46. Found: C, 67.99; H, 8.78.

11β-Hydroxy-4-pregnen-3-one-20,21-bisethylene Dioxide (3b).—A. A portion, 100 mg., of the residue obtained on reduction of the powder (a) with lithium aluminum hydride was dissolved in aqueous acetic acid (1:1) and was heated on a steam bath (1 hr.). The volatile components were removed in a stream of nitrogen, and the residue was dried under reduced pressure. The sirup was crystallized from methanol–ether to yield **3b**, 27 mg.

B. Corticosterone-21-aldehyde (hydrate) (**5**) was prepared by a sequence of reactions described by W. J. Leanza, *et al.*[14] The product gave positive tests for an aldehyde.

A mixture of the aldehyde (**5**), 400 mg., ethylene glycol, 3.6 ml., benzene, 40 ml., and *p*-toluenesulfonic acid, 20 mg., was slowly distilled during 4 hr. The reaction mixture was processed as previously described to yield a sirup, 500 mg., which was chromatographed on Woelm neutral alumina, activity II. Elution with hexane–benzene (3:2 through 1:1) gave a solid, 88 mg., which was not investigated further because its infrared spectrum was devoid of bands ascribable to hydroxyls or ketones. Elution with benzene–chloroform (99:1 through 2:3) gave a sirup, 180 mg. which was crystallized from methanol–methylene chloride. The solid was not homogeneous, and was rechromatographed on neutral alumina. Eluates of chloroform–benzene (1:19) contained a mixture of **3b** and **9b** and eluates of chloroform–benzene (1:9) gave **3b**. The mixture of **3b** and **9b** was fractionally crystallized from 95% ethanol to yield in the first crop **9b** and in the second crop **3b**.

A sample of **3b** was crystallized repeatedly from methanol–ether, m.p. 120–122°; λ_{max}^{MeOH} 242 mμ, ε 15,300; ν_{max}^{KBr} 3500, 1650, 1605, 1095, 1080 cm.$^{-1}$. N.m.r. τ 4.23, 5.00, 5.58 (11α H), 6.08, 8.54, and 8.96.

Anal. Calcd. for $C_{25}H_{36}O_6 \cdot 1/2\ H_2O$: C, 68.00; H, 8.45. Found: C, 67.83, 67.65; H, 8.37, 7.94.

11β-Hydroxy-4-androsten-17β-[4α]-[1,4;5,8]-*trans*-naphthodioxan-3-one (9b).—The sample of **9b** described above was crystallized from 95% ethanol, m.p. 145–146°; λ_{max}^{MeOH} 242 mμ, ε 15,000; ν_{max}^{KBr} 3550, 1650, 1605, 1055 cm.$^{-1}$. N.m.r. 4.33, 5.42, 6.08, 8.54, 8.96.

Anal. Calcd. for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39. Found: C, 69.59, 69.10; H, 8.55, 8.18.

4-Androsten-17β-[4α]-[1,4;5,8]-*trans*-naphthodioxane-3,11-dione (9a).—A. 5-Androsten-11-one-17β-[1,4;5,8]-*trans*-naphthodioxane-3-ethylene dioxide (**8a**); λ_{max}^{MeOH} no specific absorption in the 220–240-mμ region; ν_{max}^{KBr} 1695, 1665 (small), 1100 cm.$^{-1}$. N.m.r. τ 4.67, 5.44, 6.07, band extending from 5.96–6.63, 8.76, 9.16.

A solution of **8a**, 6.5 mg., in aqueous acetic acid (1:1), 1.5 ml., was boiled for 30 min., and the resultant **9a**, 3.5 mg., m.p. 218–220°, was recovered in the conventional manner.

B. A solution of **9b**, 6.1 mg., in pyridine, 0.1 ml., was added to a suspension of chromium trioxide, 12.2 mg., in pyridine, 0.1 ml., and the mixture was stored at room temperature for 3 hr. The steroid was recovered with ethyl acetate in the conventional manner, and the residue solidified on trituration with ethanol (m.p. 210–220°).

The infrared spectra of the crystalline solids from experiments (A) and (B) were identical to that of the authentic sample of **9a**, m.p. 221–223°, obtained from Dr. S. Bernstein.

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