the mixture was heated at 80° for 6 hr, 30 ml of a mixture of petroleum ether (bp 30–60°) and diethyl ether (2:1) was poured into the cooled reaction mixture. The precipitated copper(I) chloride–*tert*-butyl isocyanide and some unreacted Cu_2O were removed by filtration. The filtrate was subjected to distillation and the residue was distilled *in vacuo*. Each fraction was analyzed by glpc. An analytical sample was purified by preparative glpc.

I. Reaction of Methyl α-Chloroacrylate with Diethyl Ethylmalonate Caused by Cuprous Oxide–*tert*-Butyl Isocyanides.—Reaction was carried out according to the procedure mentioned above. A main product of **22** [bp 123° (4 mm Hg); yield 46%] was accompanied by several minor by-products, whose nmr spectra exhibited no signal in the olefinic region. **22** (*Anal.* Calcd for $C_{13}H_{21}O_6Cl$: C, 50.57; H, 6.86; Cl, 11.48. Found: C, 50.85; H, 6.90; Cl, 11.30.) had nmr ($CDCl_3$) τ 5.2 (1 H, ClCH<), 5.75 (4 H, 2 × OCH_2CH_3), 6.21 (3 H, OCH_3), ~7.4 (2 H, >CCH_2CHCl), 8.01 (2 H, CH_3CH_2C<), 8.78 (6 H, 2 × OCH_2CH_3), 9.16 (3 H, CH_2CH_2C<).

Registry No.—**3a**, 717-69-1; **3b**, 826-35-7; **3c**, 34185-94-9; **3d**, 13949-99-0; (1α,2β,3β)-**3e**, 34185-95-0; (1α,2α,3β)-**3e′**, 34185-96-1; **3g**, 34185-98-3; **3h**, 39821-99-3; **3i**, 34185-99-4; **6a**-i, 39822-01-0; **6a**-ii, 39822-02-1; **6b**-i, 39822-03-2; **6b**-ii, 39822-04-3; **6c**-i, 30630-39-8; **6c**-ii, 30630-38-7; **6d**-i, 39822-06-5; **6d**-ii, 39822-07-6; **6e**, 39822-08-7; **7a**-i, 39822-09-8; **7a**-ii, 39822-10-1; **7b**-i, 39822-11-2; **7b**-ii, 39822-12-3; **7c**, 39822-13-4; *trans*-**7d**, 39822-14-5; *cis*-**7d**, 39822-15-6; *cis*-**7e**, 39822-16-7; *trans*-**7e**, 39822-17-8; **7f**, 39822-18-9; **18a**, 39822-24-7; **18b**, 22650-26-6; *cis*-**18c**, 39822-26-9; *trans*-**18c**, 39822-27-0; *cis*-**18d**, 39822-28-1; *trans*-**18d**, 39822-29-2; **18e**, 39822-30-5; **18f**, 714-92-1; **18g**, 39822-32-7; *cis*-**18h**, 39822-33-8; *trans*-**18h**, 39822-34-9; *cis*-**18i**, 39822-35-0; *trans*-**18i**, 39822-36-1; *cis*-**18j**, 39822-37-2; *trans*-**18j**, 39822-38-3; **18k**, 19930-90-6; *cis*-**18l**, 39822-41-8; *trans*-**18l**, 39822-42-9; **19g** (X = Ac; R = Me), 39822-40-7; **19h** (X = EtO_2C; R = Me), 39822-43-0; **19i** (X = Ph; R = Me), 39822-44-1; **19j** (X = Ph; R = H), 39822-45-2; **19k** (X = Ac; R = Me), 39822-46-3; **22**, 39822-47-4; cuprous oxide–*tert*-butylisonitrile complex, 39822-48-5; cuprous oxide–cyclohexylisonitrile complex 39822-49-6.

Reaction of α-Ketols and Other 21-Hydroxy Steroids with Phosgene. II. Structural Requirements in the Formation of 20-Chloro-20,21-cyclic Carbonates from 11-Deoxycorticosterone and 11-Dehydrocorticosterone[1]

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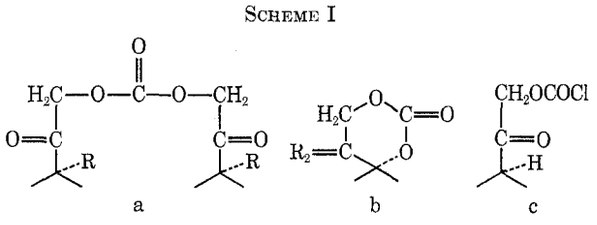
Reaction of 11-deoxycorticosterone (**1**) in pyridine with excess phosgene in benzene (condition B) affords the novel-20-chloro-20,21-cyclic carbonates **3a,b** as major products and the 21-chloride **2** as a minor product. In contrast, phosgenation of 11-dehydrocorticosterone (**9**) under condition B gives the 21-chloride **10** as a major product and the 20-chloro-20,21-cyclic carbonates **11a** and **11b** as minor products. Reduction of the 11-deoxy-cyclic chlorocarbonates **3a,b** with zinc in acetic acid furnishes both progesterone (**7**) and the epimeric 20-acetoxy-20,21-cyclic carbonates **8a** and **8b**, whereas similar reduction of **11a** and **11b** gives 11-ketoprogesterone (**12**) as the only significant product. Those structural features which are essential for cyclic chlorocarbonate formation have been determined by phosgenating under condition B a number of 17-deoxy-21-ols with various substituents at C-20. These include 11,20-dideoxycorticosterone (**16**) and the 3,20-bisethylene ketals of **1** and **9** as well as the analogous Δ^{16}-20-ketones and Δ^{16}-20-ethylene ketals. It was concluded from these studies that, although all steroidal 21-ols form 21-chlorocarbonates under condition B, hydrolysis to starting material occurs during the work-up in the absence of a carbonyl group at C-20 and a saturated D ring.

In the first paper of this series[2] we described the preparation of symmetrical and mixed 21,21′-bisteroidal carbonates (partial formula a, R = H or OH, Scheme I)

SCHEME I



by the slow addition of phosgene to excess α-ketols in pyridine (condition A). It was also reported that addition of cortisone (but not 11-deoxycortisol) and a number of nonketolic 17,21-diols to excess phosgene (condition B) affords 17,21-cyclic carbonates (partial formula b). This study has been extended to the phosgenation of 17-deoxy-α-ketols under condition B in the expectation that, in the absence of a hydroxyl group at C-17, 21-chlorocarbonates (partial formula c) would be major products. The results of this investigation, as well as a detailed examination of the influence of neighboring functional groups on reactions at C-21, are reported in the present paper.

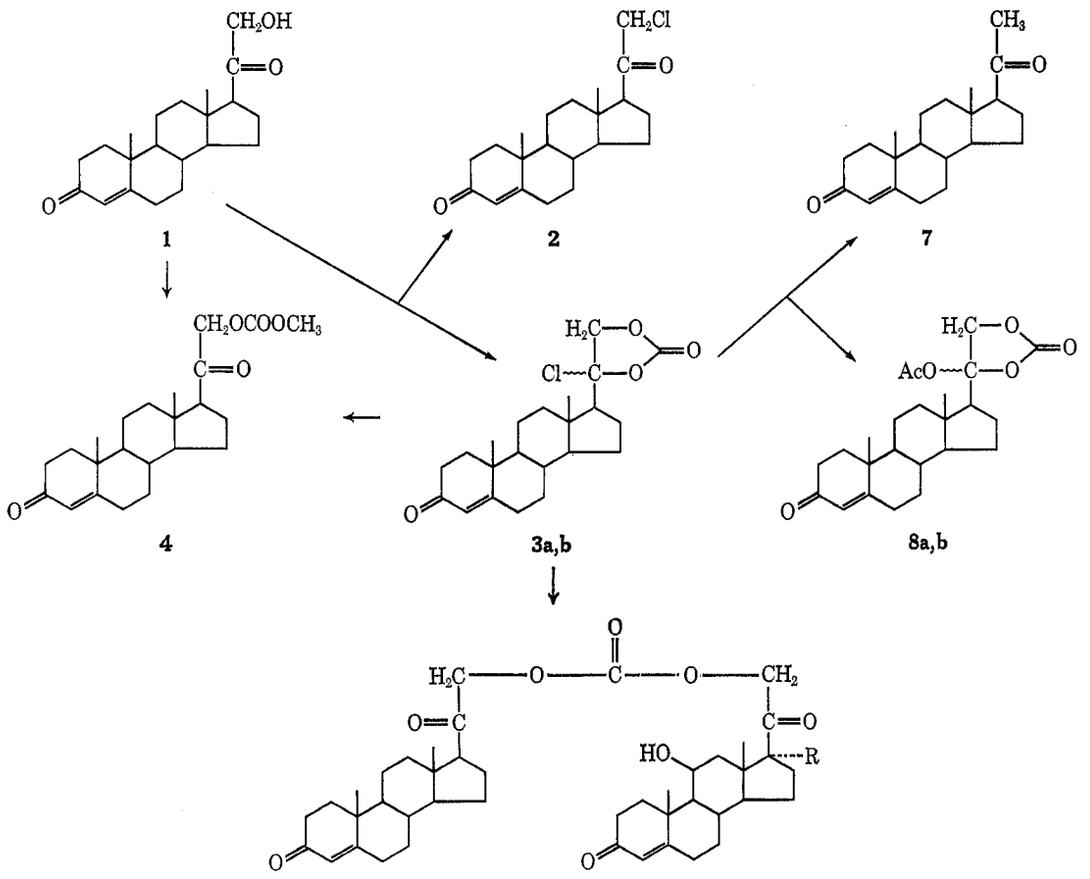
Treatment of 11-deoxycorticosterone (**1**, Scheme II) under condition B and tlc analysis of the reaction mixture showed that, in addition to small amounts of the bisteroidal carbonate and a component with the same mobility as 21-chloroprogesterone (**2**),[3] a major product with intermediate mobility is formed. The ketolic nature of the latter substance was evident from its rapid reduction of alkaline blue tetrazolium (BT). Column chromatography on silica gel gave the 21-chloride **2** in 14% yield, but resulted in nearly total destruction of the major product. It was found subsequently that repeated crystallizations from methylene chloride permitted direct isolation of this compound in 53% yield.

(1) This research was supported wholly by a grant, AM01255, from the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, U. S. Public Health Service. We are grateful to this institute for its continued and generous support of our work.

(2) M. L. Lewbart, *J. Org. Chem.*, **37**, 3892 (1972).

(3) H. Reich and T. Reichstein, *Helv. Chim. Acta*, **22**, 1124 (1939).

SCHEME II[a]



[a] In this and other schemes, the substituent at C-20 is α oriented in "a" compounds and β oriented in "b" compounds.

Since the major product is both Beilstein and BT positive, it was assumed to be the 21-chlorocarbonate. However, infrared analysis showed an intense carbonyl band at 1835 cm^{-1}, which is characteristic of five-membered ring cyclic carbonates,[4] but is of significantly higher frequency than the reported[5] range of 1780–1775 cm^{-1} for linear chlorocarbonates. The absence of a second carbonyl band near 1700 cm^{-1} (C-20 carbonyl) served further to rule out a 21-chlorocarbonate structure. Nmr analysis[6] revealed that the product is a roughly 1:1 mixture of closely related substances, as evidenced by splitting of the 18-CH_3 and 21-CH_2 signals. On the basis of these findings and the reactions to be described in this and the accompanying paper, the major phosgenation product from **1** under condition B is formulated as an epimeric mixture of 20-chloro-20,21-cyclic carbonates (**3a,b**). To our knowledge cyclic chlorocarbonates of this type have not been encountered either in the steroid or carbohydrate fields.

Isomerization of the cyclic chlorocarbonates **3a,b** to the open-chain form apparently is a necessary preliminary to reactions with alcohols, since substitution occurs only at C-21. For example, treatment of **3a,b** in pyridine at room temperature with an equivalent amount of methanol provided the 21-*O*-carbomethoxy (camylate) derivative **4** in 78% yield. The structure of **4** was confirmed by its independent synthesis from **1** by direct camylation. The synthesis of mixed carbonates of **1** with other α-ketols, which could be achieved only in low yields by phosgenating equivalent mixtures under condition A,[2] has been considerably improved by treating chlorocarbonates **3a,b** in pyridine with the appropriate substrate. For example, the mixed carbonates (**5** and **6**, respectively) of **1** with corticosterone and cortisol were recovered in yields averaging 70%. Presumably, any mixed carbonate of 11-deoxycorticosterone with a compound bearing a readily acylable hydroxyl can be prepared in this manner.

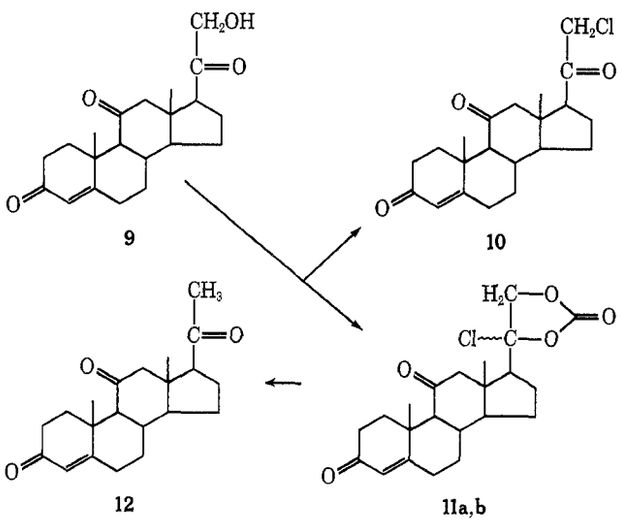
In order to obtain chemical evidence of the cyclic nature of **3a,b**, attempts were made to reduce them to halogen-free cyclic carbonates. Treatment with sodium borohydride in dimethylformamide gave a complex mixture, but reaction with zinc in acetic acid furnished what appeared to be two products. The mobile component, isolated after column chromatography on silica gel, was identified as progesterone (**7**). The more polar component was shown by spectral analyses to be a roughly 3:2 mixture of acetylated cyclic carbonates. Rechromatography on a partitioning-type column effected resolution of the mixture, and the pure components are formulated as the 20-acetoxy-20,-21-cyclic carbonates **8a** and **8b**. However, the evidence at hand does not permit individual configurational assignments. As an alternative preparative procedure the reaction mixture from **3a,b** was chromatographed directly on the partitioning column, affording pro-

(4) M. L. Lewbart, *J. Org. Chem.*, **37**, 1233 (1972).
(5) R. A. Nyquist and W. J. Potts, *Spectrochim. Acta*, **17**, 679 (1961).
(6) We wish to thank Dr. Byron H. Arison of the Merck Institute for the determination and interpretation of the nmr spectra.

gesterone (32%) and the mobile (11%) and polar (25%) acetoxy cyclic carbonates **8a** and **8b**. The presence of zinc is essential in the formation of the latter compounds, since a solution of **3a,b** in acetic acid alone is stable for at least several hours. The generation of two types of dehalogenation products from **3a,b** suggests that progesterone is formed to the extent that isomerization to the linear chlorocarbonate occurs, whereas that portion which remains cyclized undergoes direct substitution of acetate for chloride at C-20.

The phosgenation of 11-dehydrocorticosterone (**9**, Scheme III) under condition B was also studied,

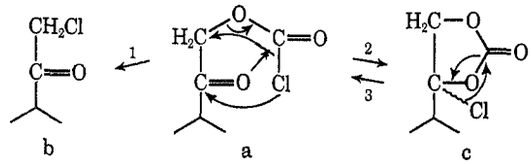
SCHEME III



Comparison of the tlc patterns of the reaction mixtures from **9** and **1** showed qualitative similarities but striking quantitative differences. In the 11-keto series the major product (subsequently isolated in 31% yield) is the 21-chloride **10**, and the cyclic chlorocarbonates are minor reaction products. In contrast to their 11-deoxy analogs **3a,b**, however, the 20-chloro-20,21-cyclic carbonates (**11a,b**) are separable on a silica gel column and, despite their limited stability under these conditions, could be isolated in pure form. Based on the nature of their dehydrohalogenation products (see accompanying paper) the more mobile component is formulated as 20β,21-cyclocarbonyldioxy-20α-chloropregn-4-ene-3,11-dione (**11b**) and the more polar component as 20α,21-cyclocarbonyldioxy-20β-chloropregn-4-ene-3,11-dione (**11a**). When **11a** and **11b** were treated with zinc in acetic acid only traces of products with the expected mobility of 20-acetoxy-20,21-cyclic carbonates were formed. The only recoverable common product from **11a** and **11b** was 11-ketoprogesterone (**12**) in yields of 40 and 48%, respectively. This finding suggests that under the reaction conditions isomerization to the linear chlorocarbonate prior to dehalogenation is more complete in the 11-keto series.

The formation of both 21-chlorides and cyclic chlorocarbonates from **1** and **9** under condition B can be understood in terms of a four-center type mechanism analogous to that proposed to explain the generation of a 20-methoxy-17,20-cyclic carbonate from a 17α-camyl-20-one.[2] There is little doubt that 21-chlorocarbonate a (Scheme IV) is the primary product. Decarboxylation of a, which has been shown to proceed by this

SCHEME IV



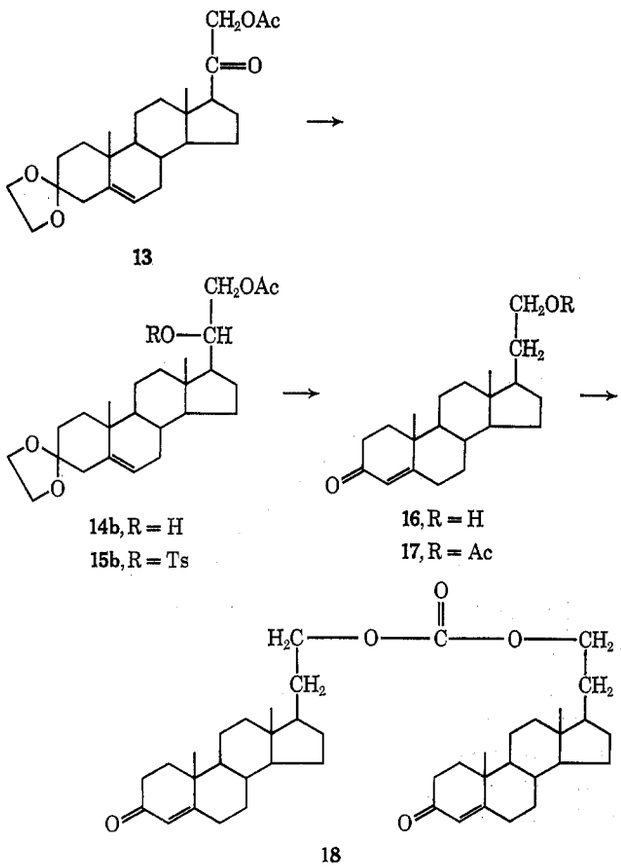
mechanism,[7] affords the alkyl chloride b *via* pathway 1. If, however, attack by the C-20 carbonyl oxygen on the carbonate carbonyl occurs in conjunction with migration of chloride to C-20 (pathway 2), cyclic chlorocarbonate c results. The ready reversal of pathway 2, which results from attack by chloride on the carbonate carbonyl with simultaneous regeneration of the 20-carbonyl group (pathway 3), is evident from the nature of the C-21-substituted products previously discussed. In comparing the reactions of **1** and **9** under condition B, it is also evident that the presence of a carbonyl group at C-11 favors pathway 1, since the yield of the 11-keto 21-chloride **10** is more than twice that of its 11-deoxy analog **2**. Because free rotation is possible between all bonds in the side chain of the linear chlorocarbonate c, it is not surprising that random attack by chloride at C-20 in pathway 2 affords both possible cyclic chlorocarbonates.

The nature of phosgenation products from 17-deoxy-21-ols with substituents other than a carbonyl group at C-20 has also been examined. It was hoped that, if cyclic chlorocarbonate formation is precluded, stable 21-chlorocarbonates could be recovered. A synthesis of the simplest representative of this series, 11,20-dideoxycorticosterone (**16**, Scheme V) was therefore undertaken. Reduction of the ketal 21-acetate **13** with sodium borohydride in methanol afforded the 20β-hydroxy-21-acetate **14b**[8] in a yield of 79%. Conversion of **14b** to its 20β-tosyl derivative **15b**[8] (83% yield) followed by successive lithium aluminum hydride reduction and acid hydrolysis furnished the desired 20-deoxy-21-ol **16** in 40% yield. Phosgenation of **16** under condition B followed by the usual work-up (which involves addition of ice to the reaction mixture) gave starting material only. In order further to assess the reactivity of **16**, it was also phosgenated under condition A. There resulted an only modest yield (48%) of bisteroidal carbonate **18**, and a substantial amount (24%) of **16** was also recovered. It is evident that under both conditions the 21-chlorocarbonate is a major product, but under circumstances where cyclization is not possible, it is rapidly hydrolyzed to the parent 21-ol during the work-up.

Another pair of 21-ols, the 3,20-bisketals from 11-deoxycorticosterone[9] and 11-dehydrocorticosterone[10] (**19** and **20**, Scheme VI), were also subjected to phosgenation. As in the case of **16**, treatment of **19** and **20** under condition B resulted in their nearly quantitative recovery from the reaction mixture. That 21-chlorocarbonate formation does occur was shown in a separate experiment by adding methanol instead of ice, whereby the 21-camylates **21** and **22** could be isolated in

(7) J. Hine, "Physical Organic Chemistry," McGraw-Hill, New York, N. Y., 1956, p 458.
(8) D. N. Kirk and F. J. Rowell, *J. Chem. Soc. C*, 1498 (1970).
(9) J. von Euw, R. Neher, and T. Reichstein, *Helv. Chim. Acta*, **38**, 1423 (1955).
(10) S. Bernstein and R. H. Lenhard, *J. Amer. Chem. Soc.*, **77**, 2331 (1955).

SCHEME V

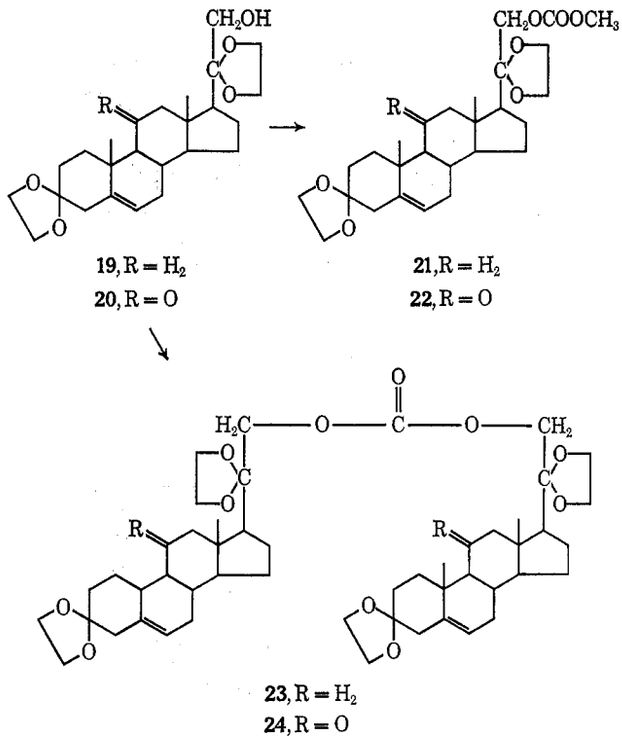


yields of 80 and 85%, respectively. Since treatment of bisketals **19** and **20** under condition A afforded the corresponding bisteroidal carbonates **23** and **24** in very low yields (9 and 24%, respectively), it is evident here also that, in the absence of a 20-carbonyl, 21-chlorocarbonate formation predominates.

It also seemed of interest to investigate Δ^{16} compounds analogous to **1** and **9** in order to determine what influence the proximity of a double bond has on the reaction of α-ketols with phosgene. Reaction of Δ^{16}-α-ketols **25** and **26** (Scheme VII) under condition B followed by the usual work-up furnished crude products whose infrared spectra closely resembled those of starting material, although weak bands at 1820, 1760, and 1730 cm^{-1}, characteristic of cyclic chlorocarbonates, bisteroidal carbonates, and 20-oxo-21-chlorides, respectively, were also noted. These results indicate that the presence of a C-16–C-17 double bond greatly inhibits cyclization of α-ketol 21-chlorocarbonates. There is no question that 21-chlorocarbonates are formed, since in a separate experiment addition of ethanol to reaction mixtures from **25** and **26** gave the 21-cathylates **27** and **28** in respective yields of 60 and 52%. Treatment of **25** and **26** under condition A provided their respective bisteroidal carbonates **29** and **30** in yields of 56 and 68%. As an extension of this study, the 3,20-bisketals (**37** and **38**) derived from **25** and **26** were also subjected to phosgenation conditions. For their preparation the 3,20-bisketal 21-acetates (**31** and **32**) from 11-deoxycortisol[11] and cortisone[12] were treated with thionyl chloride in

(11) R. Antonucci, S. Bernstein, and R. H. Lenhard, *ibid.*, **76**, 2956 (1954).
(12) R. Antonucci, S. Bernstein, M. Heller, R. H. Lenhard, R. Littell, and J. H. Williams, *J. Org. Chem.*, **18**, 70 (1953).

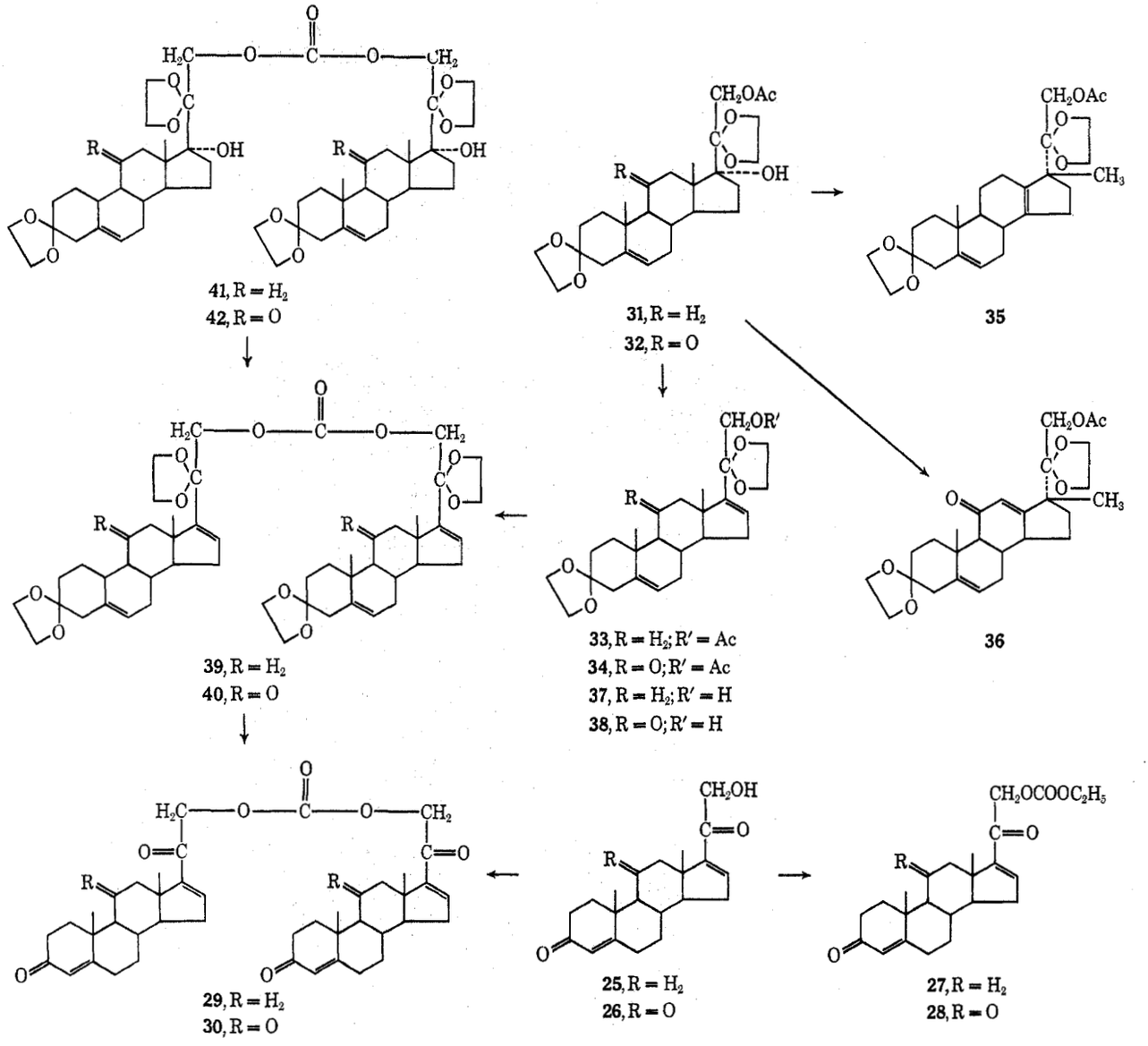
SCHEME VI



pyridine under conditions similar to those used by Bernstein, *et al.*[13] In addition to the normal dehydration products **33** and **34**, which were obtained in yields of 41 and 75%, respectively, an isomeric by-product was also recovered from each reaction mixture. These have been formulated respectively as the $\Delta^{13,14}$- and $\Delta^{12,13}$-18-nor Wagner–Meerwein products **35** and **36**. The latter structural assignment was based on the observation that this by-product absorbs strongly in the ultraviolet region.[14] The formation of these rearrangement products serves in part to account for the modest yields of Δ^{16}-20-ketals reported by Bernstein, *et al.*,[13] in dehydrations of several 17α-ols. Phosgenation under A of **37** and **38**, obtained by saponification of **33** and **34**, furnished the corresponding bisteroidal carbonates **39** and **40** in yields of 81 and 75%, respectively. When these yields are contrasted with those of their D ring-saturated counterparts **23** and **24**, it is evident that the presence of the double bond exerts a beneficial influence on bisteroidal carbonate formation from 20-ethylenedioxy-21-ols. Correlation of **39** and **40** with the previously described[2] 17α-ols **41** and **42** was also sought. Treatment of the bis-11-one **42** with thionyl chloride in pyridine gave **40** in 76% yield. However, similar reaction of **41** afforded **39** as a minor product (8%). The major dehydration product (30%) is tentatively formulated as a Wagner–Meerwein product of bisteroidal carbonate **39**. When the behavior of the monomeric 21-acetate **33** and the bisteroids **41** and **42** under dehydration conditions are compared, it is apparent that the presence of a 21,21′-carbonate linkage in the absence of a carbonyl at C-11 favors generation of the abnormal product. The much greater resistance to mineral acids of carbonate over ethylene ketal bonds was demonstrated by the ready hydrolysis in methanolic sulfuric

(13) W. S. Allen and S. Bernstein, *J. Amer. Chem. Soc.*, **77**, 1028 (1955).
(14) N. L. Wendler, R. P. Graber, and G. G. Hazen, *Tetrahedron*, **3**, 144 (1958).

SCHEME VII



acid of the bisketal carbonates **39** and **40** to **29** and **30** in excellent yields.

It can be concluded from the experiments described in this and the preceding communication[2] that all steroidal 21-ols readily form 21-chlorocarbonates under condition B. However, only starting material will be recovered after the usual work-up in the absence of additional structural features which permit cyclization to stable products. The two features encountered thus far are (a) the presence of a 17α-hydroxyl leading to 17,21-cyclic carbonates, and (b) the presence of both a saturated D ring and C-20 carbonyl which provides cyclic chlorocarbonates.

The infrared spectral properties of the new cyclic chlorocarbonates **3a,b**, **11a**, and **11b** may be briefly summarized as follows. All three exhibit carbonate carbonyl bands ranging from 1836 to 1833 cm^{-1}. In addition they possess strong to very strong bands at 1282–1275, 1173–1165, 1065–1060, and 769–766 cm^{-1}.

Experimental Section

Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Optical rotations were determined at 589 mμ (D line of sodium) in a Zeiss 0.005° photoelectric polarimeter. Unless noted otherwise, measurements were made in chloroform solution in a 0.5-dm tube at a concentration of about 1% and at a temperature of 26 ± 1°. Infrared (ir) spectra were determined as KBr pellets with a Beckman IR-8 instrument. Nmr spectra were determined with a Varian HA-100D instrument in $CDCl_3$, using TMS as an internal standard. Ultraviolet (uv) spectra were obtained in methanol solution with a Zeiss PRQ 20A recording spectrophotometer. General procedures for chromatographic techniques on silica gel, including column dimensions, fraction size, and flow rate, as well as the processing of reaction mixtures, follow from earlier publications.[15] Unless otherwise indicated, tlc and column systems are indicated in the text by a number which corresponds to one of the following compositions [in each case the number is followed (in parentheses) by that volume of ethyl acetate which, diluted to 25 ml with isooctane (or, in the cases of systems 7, 8, and 9, with toluene), comprises the system]: 1 (10), 2 (12.5), 3 (8.8), 4 (15), 5 (13.8), 6 (7.5), 7 (3.1), 8 (6.2), 9 (7.5). Microanalyses were by A. Bernhard, Elbach über Engelskirchen, West Germany.

Phosgenation of 11-Deoxycorticosterone (1) under Condition B.—Repeated crystallizations from methylene chloride of the reaction mixture from 3.3 g (10 mmol) of steroid afforded 2.07 g (53%) of **20ξ,21-cyclocarbonyldioxy-20ξ-chloropregn-4-en-3-one (3a,b)**: mp 159–160°; $[\alpha]_D$ +109°; λ_{max} 241 mμ (ϵ 16,800); ν_{max} 1835 cm^{-1} (cyclic carbonate); nmr δ 9.13 and 9.03 (s, 3,

(15) M. L. Lewbart and J. J. Schneider, *J. Org. Chem.*, **34**, 3505 (1969).

18-CH_3), 8.81 (s, 3, 19-CH_3), 5.43, 5.34, and 5.37, 5.29 (d, 2, J = 10.0 Hz, 21-CH_2).

Anal. Calcd for $C_{22}H_{29}O_4Cl$: C, 67.25; H, 7.44; Cl, 9.02. Found: C, 67.13; H, 7.47; Cl, 8.87.

The mother liquor was chromatographed on a silica gel column in system 1. This furnished **21-chloropregn-4-ene-3,20-dione** (2) as plates from ethyl acetate (470 mg, mp 204–205°; 25 mg, mp 200–201°) in a yield of 14%: $[\alpha]_D$ +220°; λ_{max} 240 mμ (ε 16,400) [lit.[8] mp 203–205°; $[\alpha]_D$ +210°; λ_{max} 242 mμ (log ε 4.15)].

21-*O*-Carbomethoxypregn-4-ene-3,20-dione (4) from 3a,b.—To a solution of 20ξ,21-cyclocarbonyldioxy-20ξ-chloropregn-4-en-3-one (79 mg, 0.2 mmol) in pyridine (1 ml) was added 85 μl (0.21 mmol) of methanol. After 66 hr at room temperature the product was recovered and crystallized from methanol as needles (48 mg, mp 160–162°; 12 mg, mp 155–158°) in a yield of 78%: $[\alpha]_D$ +196°; λ_{max} 240 mμ (ε 16,650); γ_{max} 1759, 1280, and 798 cm^{-1} (camylate).

Anal. Calcd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30; CH_3O, 7.99. Found: C, 71.19; H, 8.39; CH_3O, 8.03.

Treatment of 11-deoxycorticosterone (100 mg) in pyridine (1 ml) with methyl chlorocarbonate (75 μl) for 1 hr at room temperature afforded 110 mg (94%) of prisms from methanol, mp 156–158°. The ir spectrum was identical with that of the 21-camylate (4) prepared from **3a,b**.

3,20-Dioxopregn-4-en-21-yl 11β-Hydroxy-3,20-dioxopregn-4-en-21-yl Carbonate (5) from 3a,b.—A mixture of 20ξ,21-cyclocarbonyldioxy-20ξ-chloropregn-4-en-3-one (393 mg, 1 mmol) and corticosterone (381 mg, 1.1 mmol) was dissolved with slight warming in 1:1 pyridine–methylene chloride (6 ml). After 66 hr at room temperature the product was recovered and crystallized as rosettes from methanol (503 mg, mp 134–138°) in a yield of 68%. The ir spectrum was identical with that of the mixed carbonate prepared by phosgenating equivalent mixtures of the two α-ketols under condition A.[2]

3,20-Dioxopregn-4-en-21-yl 11β,17-Dihydroxy-3,20-dioxopregn-4-en-21-yl Carbonate (6) from 3a,b.—Treatment of 20ξ,21-cyclocarbonyldioxy-20ξ-chloropregn-4-en-3-one with cortisol (402 mg 1.1 mmol) as in the preparation of **5** from **3a,b** afforded 551 mg, (71%) of needles from methanol, mp 154–156°, whose ir spectrum was identical with that of **6** prepared by phosgenation of the parent α-ketols.[2]

Reaction of 20ξ,21-Cyclocarbonyldioxy-20ξ-chloropregn-4-en-3-one (3a,b) with Zinc in Acetic Acid.—A solution of the chlorocarbonates (590 mg) in 3:1 acetic acid–methylene chloride (20 ml) was shaken with powdered zinc (1.2 g) for 1 hr. The insoluble material was filtered off and washed with acetone. The filtrate was concentrated nearly to dryness in a nitrogen stream, then partitioned between methylene chloride and dilute sodium bicarbonate. The reaction mixture was chromatographed on a Celite column in the system toluene–isooctane–formamide (95:205:20). Crystallization of the most mobile component from acetone–hexane gave prisms (117 mg, mp 130–131°; 35 mg, mp 127–129°) in a yield of 32%. The ir spectrum was indistinguishable from that of a reference sample of **progesterone** (7).

The intermediate fraction furnished the "mobile" **20ξ,21-cyclocarbonyldioxy-20ξ-acetoxypregn-4-en-3-one** as prisms from ethyl acetate (60 mg, mp 246–247°; 10 mg, mp 243–244°) in a yield of 11%: $[\alpha]_D$ +123°; λ_{max} 241 mμ (ε 17,300); ν_{max} 1820 (cyclic carbonate), 1760, 1225 cm^{-1} (acetate); nmr δ 9.07 (s, 3, 18-CH_3), 8.82 (s, 3, 19-CH_3), 7.89 (s, 3, CH_3CO), 5.63, 5.37 (q, 2, J = 10.5 Hz, 21-CH_2).

Anal. Calcd for $C_{24}H_{32}O_6$: C, 69.21; H, 7.75; CH_3CO, 10.33. Found: C, 69.37; H, 7.58; CH_3CO, 10.17.

The least mobile fraction supplied the "polar" **20ξ,21-cyclocarbonyldioxy-20ξ-acetoxypregn-4-en-3-one** as prisms from ethyl acetate (138 mg, mp 247–247.5°; 18 mg, mp 243–244°) in a yield of 25%: $[\alpha]_D$ +104°; λ_{max} 241 mμ (ε 18,000); ν_{max} 1820 (cyclic carbonate), 1760, 1225 cm^{-1} (acetate); nmr δ 9.18 (s, 3, 18-CH_3), 8.82 (s, 3, 19-CH_3), 7.89 (s, 3, CH_3CO), 5.45 (s, 2, 21-CH_2).

Anal. Calcd for $C_{24}H_{32}O_6$: C, 69.21; H, 7.75; CH_3CO, 10.33. Found: C, 69.06; H, 7.82; CH_3CO, 10.44.

Phosgenation of 11-Dehydrocorticosterone (9) under Condition B.—The reaction mixture from 1032 mg (3 mmol) of steroid was chromatographed on a silica gel column in system 4. Crystallization of the most mobile component from acetone gave **21-chloropregn-4-ene-3,11,20-trione** (10) as prisms (334 mg, mp 185–186.5°) in a yield of 31%: $[\alpha]_D$ +279°; λ_{max} 238 mμ (ε 15,800); ν_{max} 1731 cm^{-1} (20-ketone).

Anal. Calcd for $C_{21}H_{27}O_3Cl$: C, 69.50; H, 7.50; Cl, 9.77. Found: C, 69.68; H, 7.57; Cl, 9.78.

Two crystallizations from ethyl acetate of the intermediate fraction afforded **20β,21-cyclocarbonyldioxy-20α-chloropregn-4-ene-3,11-dione (11b)** as prisms (83 mg, 7%): mp 154.5–156°; $[\alpha]_D$ +193°; λ_{max} 238 mμ (ε 16,500); ν_{max} 1832 cm^{-1} (cyclic carbonate); nmr δ 9.17 (s, 3, 18-CH_3), 8.60 (s, 3, 19-CH_3), 7.20, 7.07 (d, 1, 12β H), 5.35 (s, 2, 21-CH_2).

Anal. Calcd for $C_{22}H_{27}O_5Cl$: C, 64.93; H, 6.69; Cl, 8.71. Found: C, 64.83; H, 6.58; Cl, 8.82.

The least mobile fraction gave, after two crystallization from ethyl acetate, 124 mg (10%) of **20α,21-cyclocarbonyldioxy-20β-chloropregn-4-ene-3,11-dione (11a)** as needles: mp 165–166°; $[\alpha]_D$ +146°; λ_{max} 237 mμ (ε 16,200); ν_{max} 1832 cm^{-1} (cyclic carbonate); nmr δ 9.05 (s, 3, 18-CH_3), 8.59 (s, 3, 19-CH_3), 7.04, 6.91 (d, 1, 12β H), 5.47, 5.34 (q, 2, J = 10.0 Hz, 21-CH_2).

Anal. Calcd for $C_{22}H_{27}O_5Cl$: C, 64.93; H, 6.69; Cl, 8.71. Found: C, 64.79; H, 6.64; Cl, 8.61.

Pregn-4-ene-3,11,20-trione (12) from 11a and 11b.—Solutions of 40 mg each of 20α,21-cyclocarbonyldioxy-20β-chloropregn-4-ene-3,11-dione and 20β,21-cyclocarbonyldioxy-20α-chloropregn-4-ene-3,11-dione in 3:1 acetic acid–methylene chloride (1.6 ml) were shaken with 80 mg of powdered zinc for 45 min. The crude products, recovered as in the reaction of **3a,b**, were chromatographed on Celite columns in the system toluene–isooctane–formamide (100:100:5). The major product from **11a** was obtained as prisms from methanol (10.1 mg, mp 176–177°; 2.9 mg, mp 173–175°) in a yield of 40%. The ir spectrum was identical with that of **11-ketoprogesterone** (12). Similarly, **11b** gave 15.4 mg (48%) of prisms, mp 177–178°; which possessed an ir spectrum identical with that of the reference compound. Continued development of both columns furnished only traces of BT-positive compounds.

3-Ethylenedioxypregn-5-ene-20β,21-diol 21-Acetate (14b) from 13.—To a solution of 21-acetoxypregn-5-ene-3,20-dione 3-ethylene ketal[16] (4.16 g, 10 mmol) in a mixture of methylene chloride (150 ml) and methanol (250 ml) at 0° was added sodium borohydride (600 mg, 16 mmol). After 20 min at 0° acetic acid (1.2 ml) was added and, after concentration of the solution to a small volume, the product was recovered by extraction with methylene chloride. Two crystallizations from methanol gave 3.29 g (79%) of needles: mp 157–158.5°; $[\alpha]_D$ −30.3°; ν_{max} 3510 (hydroxyl), 1741 and 1250 (acetate), and 1100 cm^{-1} (ketal) [lit.[8] mp 145–149°; $[\alpha]_D$ −12° (dioxane)].

Anal. Calcd for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.75; H, 9.11.

3-Ethylenedioxypregn-5-ene-20β,21-diol 20-Tosylate 21-Acetate (15b) from 14b.—To a solution of 3-ethylenedioxypregn-5-ene-20β,21-diol 21-acetate (3 g) in pyridine (15 ml) was added an equal weight of tosyl chloride. After 68 hr at room temperature the product was recovered in the usual manner and crystallized from acetone as platelets (3.36 g, mp 146.5–147.5°) in a yield of 83%: $[\alpha]_D$ −17.3°; ν_{max} 1748, 1235 (acetate), 1603, 1500, 1360, 1192, 1178, 681 (tosylate),[17] 1100 cm^{-1} (ketal) (lit.[8] no constants given).

Anal. Calcd for $C_{32}H_{44}O_7S$: C, 67.10; H, 7.74. Found: C, 67.04; H, 7.85.

21-Hydroxypregn-4-en-3-one (16) from 15b.—A solution of 3 g each of 3-ethylenedioxypregn-5-ene-20β,21-diol 20-tosylate 21-acetate and lithium aluminum hydride in tetrahydrofuran (190 ml) was refluxed for 2 hr and the crude product (1.6 g) was treated with 10:1 methanol–8% sulfuric acid (55 ml) for 19 hr at room temperature. The reaction mixture was chromatographed on a silica gel column in system 2. A mobile by-product crystallized from acetone as needles (142 mg, mp 160–163°) in a yield of 8.5%. Its ir spectrum was identical with that of a reference sample of **20α-hydroxypregn-4-en-3-one**. The major product (**16**) was obtained as needles from ether and ethyl acetate–*n*-hexane (450 mg, mp 125–127°; 200 mg, mp 121–122.5°) in 40% yield: $[\alpha]_D$ +132°; λ_{max} 242 mμ (ε 16,600); ν_{max} 3440 cm^{-1} (hydroxyl).

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19. Found: C, 79.83; H, 10.30.

Treatment of **16** with acetic anhydride–pyridine and crystallization of the product from *n*-hexane afforded **21-acetoxypregn-4-**

(16) R. Antonucci, S. Bernstein, R. H. Lenhard, K. J. Sax, and J. H. Williams, *J. Org. Chem.*, **17**, 1369 (1952).

(17) M. L. Lewbart, *ibid.*, **33**, 1695 (1968).

en-3-one (17) as prisms: mp 118.5–119°; $[\alpha]D$ +112°; λ_{max} 241 mμ (ε 16,600); ν_{max} 1731, 1235 cm^{-1} (acetate).

Anal. Calcd for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 76.94; H, 9.59.

Bis(3-oxopregn-4-en-21-yl) Carbonate (18) from 16.—Phosgenation of 21-hydroxypregn-4-en-3-one (158 mg, 0.5 mmol) was carried out under condition A. Two crystallizations of the product from methanol gave 72 mg of needles: mp 193–195°; $[\alpha]D$ +124°; λ_{max} 241 mμ (ε 32,000); ν_{max} 1745, 1266, and 785 cm^{-1} (bisteroidal carbonate).

Anal. Calcd for $C_{48}H_{62}O_5$: C, 78.37; H, 9.48. Found: C, 78.56; H, 9.57.

The mother liquor was chromatographed on a silica gel column in system 2. Following the recovery of an additional 8 mg of **18**, mp 186–190° (raising the yield of 48%), there was obtained 38 mg (24%) of starting material (**16**), mp 131–132°.

21-*O*-Carbomethoxypregn-5-ene-3,20-dione 3,20-Bisethylene Ketal (21) from 19.—Phosgenation of 21-hydroxypregn-5-ene-3,20-dione 3,20-bisethylene ketal[9] (84 mg, 0.2 mmol) under condition B was followed by addition of methanol (1 ml). Crystallization of the product from ethyl acetate gave 76 mg (80%) of prisms: mp 182–184°; $[\alpha]D$ −21.5°; ν_{max} 1755, 1265, and 791 (camylate), 1101 cm^{-1} (ketal).

Anal. Calcd for $C_{27}H_{40}O_7$: C, 68.04; H, 8.46. Found: C, 68.20; H, 8.26.

21-*O*-Carbomethoxypregn-5-ene-3,11,20-trione 3,20-Bisethylene Ketal (22) from 20.—Phosgenation of 21-hydroxypregn-5-ene-3,11,20-trione 3,20-bisethylene ketal[10] (86 mg, 0.2 mmol) under condition B was followed by addition of methanol (1 ml). Crystallization from methanol furnished 83 mg (85%) of prisms: mp 166–167°; $[\alpha]D$ +5.5°; ν_{max} 1754, 1265, and 791 (camylate), 1100 cm^{-1} (ketal).

Anal. Calcd for $C_{27}H_{38}O_8$: C, 66.10; H, 7.81. Found: C, 66.27; H, 7.64.

Bis(3,20-bisethylenedioxypregn-5-en-21-yl) Carbonate (23) from 19.—The product from phosgenation of 21-hydroxypregn-5-ene-3,20-dione 3,20-bisethylene ketal (168 mg, 0.4 mmol) under condition A was chromatographed on a silica gel column in system 3. The desired product crystallized from ethyl acetate as needles (15 mg, mp 253–254°) in a yield of 9%: $[\alpha]D$ −17.7°; ν_{max} 1755, 1260, and 788 (bisteroidal carbonate), 1097 cm^{-1} (ketal).

Anal. Calcd for $C_{51}H_{74}O_{11}$: C, 70.97; H, 8.64. Found: C, 70.79; H, 8.52.

Bis(3,20-bisethylenedioxy-11-oxopregn-5-en-21-yl) Carbonate (24) from 20.—Treatment of 21-hydroxypregn-5-ene-3,11,20-trione 3,20-bisethylene ketal (173 mg, 0.4 mmol) as in the preparation of **23** from **19** and chromatography in system 5 gave 42 mg (24%) of needles from ethyl acetate: mp 286–287°; $[\alpha]D$ +1.21°; ν_{max} 1758, 1260, and 788 (bisteroidal carbonate), 1100 cm^{-1} (ketal).

Anal. Calcd for $C_{51}H_{70}O_{13}$: C, 68.74; H, 7.92. Found: C, 68.77; H, 7.70.

21-*O*-Carboethoxypregna-4,16-diene-3,20-dione (27) from 25.—Phosgenation of 21-hydroxypregna-4,16-diene-3,20-dione[13] (66 mg) under condition B was followed by addition of excess ethanol. The crude product was chromatographed on a silica gel column (system 1). The major component crystallized from methanol as needles (48 mg, mp 147.5–148.5°) in a yield of 60%: $[\alpha]D$ +147°; λ_{max} 240 mμ (ε 26,600); ν_{max} 1740, 1265, and 797 (cathylate), 1675 (C-3 and C-20 ketones), 1621 (Δ^4), 1588 cm^{-1} (Δ^{16}).

Anal. Calcd for $C_{24}H_{32}O_5$: C, 71.97; H, 8.05. Found: C, 72.10; H, 8.20.

Treatment of **25** (15 mg) in cold pyridine (0.5 ml) with ethyl chlorocarbonate (25 μl) for 2 hr at 5° and crystallization of the product from methanol gave 10.3 mg of needles, mp 149–150°. The ir spectrum was identical with that of the 21-cathylate **27** recovered after addition of ethanol to the phosgenation mixture.

21-*O*-Carboethoxypregna-4,16-diene-3,11,20-trione (28) from 26.—The crude product obtained after phosgenation of 21-hydroxypregna-4,16-diene-3,11,20-trione (68 mg) and addition of ethanol was chromatographed on a silica gel column in system 4. The major component crystallized from ethanol as needles (41 mg, mp 169–170°; 3 mg, mp 166–168°) in a yield of 52%: $[\alpha]D$ +222°; λ_{max} 238 mμ (ε 24,800); ν_{max} 1752, 1265, and 793 (cathylate), 1675 (C-3 and C-20 ketones), 1618 (Δ^4), 1591 cm^{-1} (Δ^{16}).

Anal. Calcd for $C_{24}H_{30}O_6$: C, 69.58; H, 7.30. Found: C, 69.66; H, 7.34.

Treatment of **26** (15 mg) as in the cathylation of **25** afforded 13.4 mg of prisms from ethanol, mp 167–169°, whose ir spectrum was indistinguishable from that of the 21-cathylate **28** prepared *via* the 21-chlorocarbonate.

Reaction of 21-Acetoxy-17-hydroxypregn-5-ene-3,20-dione Bisethylene Ketal (31) with Thionyl Chloride in Pyridine.—To a solution of the bisketal acetate[11] (500 mg) in pyridine at −5° was added 2 ml of thionyl chloride. After 30 min at −12° the reaction mixture was carefully added to ice and water. Methylene chloride extraction of the resulting suspension followed by successive washing with dilute hydrochloric acid, 2 *N* sodium hydroxide, and water gave the crude, neutral product. Several crystallizations from ether furnished **21-acetoxypregna-5,16-diene-3,20-dione bisethylene ketal (33)** as needles, 174 mg, mp 131–132° (lit.[13] mp 131–132°). When the mother liquor was chromatographed on a silica gel column in system 7, only partial separation of the two components was achieved. The most mobile fraction gave an additional 25 mg of **33**, mp 131–133°, raising the yield to 41%.

Several crystallizations from methanol of the residue (156 mg) from later eluates supplied 105 mg (30%) of **21-acetoxy-17β-methyl-18-nor-17α-pregna-5,13(14)-diene-3,20-dione bisethylene ketal (35)** as prisms: mp 112.5–114.5°; $[\alpha]D$ −118°; ν_{max} 1739, 1250 (acetate), 1102 cm^{-1} (ketal).

Anal. Calcd for $C_{27}H_{38}O_6$: C, 70.71; H, 8.35. Found: C, 70.80; H, 8.35.

Reaction of 21-Acetoxy-17-hydroxypregn-5-ene-3,11,20-trione 3,20-Bisethylene Ketal (32) with Thionyl Chloride in Pyridine.—Dehydration of the bisketal acetate[12] (2 g) in pyridine (40 ml) with thionyl chloride (8 ml) was carried out for 3 hr at 5°. Crystallization of the product, recovered as in the preparation of **33** and **35** from **31**, gave **21-acetoxypregna-5,16-diene-3,11,20-trione 3,20-bisethylene ketal (34)** as prisms from methanol, 1.23 g, mp 116–117.5° (lit.[13] mp 114–115°). The mother liquor was chromatographed on a silica gel column in systems 8 and 9. The initial fraction gave an additional 0.19 g of **34**, mp 116–117.5°, raising the yield to 75%. Crystallization of the less mobile component afforded **21-acetoxy-17β-methyl-18-nor-17α-pregna-5,12(13)-diene-3,11,20-trione 3,20-bisethylene ketal (36)** as needles from ethyl acetate-*n*-hexane (122 mg, mp 119.5–122°) in 6% yield: $[\alpha]D$ −110°; λ_{max} 241 mμ (ε 10,400); ν_{max} 1741, 1240 (acetate), 1654 (conjugated 11-ketone), 1109 cm^{-1} (ketal).

Anal. Calcd for $C_{27}H_{36}O_7$: C, 68.62; H, 7.68. Found: C, 68.64; H, 7.61.

Bis(3,20-bisethylenedioxypregna-5,16-dien-21-yl) Carbonate (39) from 37.—Phosgenation of 21-hydroxypregna-5,16-diene-3,20-dione bisethylene ketal[11] (166 mg, 0.4 mmol) under condition A and crystallization of the product from methanol gave needles (139 mg, mp 194.5–195.5°) in a yield of 81%: $[\alpha]D$ −43.5°; ν_{max} 1758, 1260, and 788 (bisteroidal carbonate), 1622 (Δ^{16}), 1100 cm^{-1} (ketal).

Anal. Calcd for $C_{51}H_{70}O_{11}$: C, 71.30; H, 8.21. Found: C, 71.11; H, 8.15.

39 from 41.—To a solution of bis(17-hydroxy-3,20-bisethylenedioxypregn-5-en-21-yl) carbonate[2] (200 mg) in pyridine (4 ml) at −12° was added 0.8 ml of thionyl chloride. After 30 min at −12° the product was recovered as described previously and chromatographed on a silica gel column (system 6).

The major product, which is formulated as **bis(17β-methyl-3,-20-bisethylenedioxy-18-nor-17α-pregna-5,13(14)-dien-21-yl) carbonate**, was eluted first. Crystallization from methanol gave fine needles (53 mg, mp 131–134°) in a yield of 30%; $[\alpha]D$ −95°; ν_{max} 1755, 1260, and 788 (bisteroidal carbonate), 1100 cm^{-1} (ketal).

Anal. Calcd for $C_{51}H_{70}O_{11}$: C, 71.30; H, 8.21. Found: C, 71.15; H, 8.00.

The minor product, which followed, crystallized from methanol as needles (16 mg, mp 193–194°). The ir spectrum was identical with that of **39** prepared by phosgenation of **37** under condition A.

Bis(3,20-bisethylenedioxy-11-oxopregna-5,16-dien-21-yl) Carbonate (40) from 38.—Phosgenation of 21-hydroxypregna-5,16-diene-3,11,20-trione 3,20-bisethylene ketal[12] (172 mg, 0.4 mmol) under condition A and two crystallizations of the product from methylene chloride–methanol gave 133 mg (75%) of needles: mp 179–184°; $[\alpha]D$ −13.1°; ν_{max} 1758, 1265, and 788 (bisteroidal carbonate), 1625 (Δ^{16}), 1098 cm^{-1} (ketal).

Anal. Calcd for $C_{51}H_{66}O_{13}$: C, 69.05; H, 7.50. Found: C, 68.94; H, 7.50.

40 from 42.—To a solution of bis(17-hydroxy-3,20-bisethylenedioxy-11-oxopregn-5-en-21-yl) carbonate[2] (200 mg) in pyridine (4 ml) at −12° was added 0.8 ml of thionyl chloride. After 3 hr at 5° the product was recovered in the usual manner and crystallized from methanol, affording 147 mg (76%) of needles, mp 165–166°. A mixture melting point with **40** prepared by phosgenation of **38** was 168–174° and their ir spectra were identical.

Bis(3,20-dioxopregna-4,16-dien-21-yl) Carbonate (29) from 25.—Phosgenation of 21-hydroxypregna-4,16-diene-3,20-dione (66 mg, 0.2 mmol) under condition A followed by tlc analysis showed approximately 40% of starting material. The reaction mixture was therefore rephosgenated, and the recovered material was crystallized from methanol as plates (44 mg, mp 238–240°) in a yield of 65%: $[\alpha]_D$ +152°; λ_{max} 240 mμ (ε 44,700); ν_{max} 1760, 1275, and 792 (bisteroidal carbonate), 1670 (C-3 and C-20 ketone), 1619 (Δ^4), 1590 cm^{-1} (Δ^{15}).

Anal. Calcd for $C_{43}H_{54}O_7$: C, 75.63; H, 7.97. Found: C, 75.85; H, 8.10.

29 from 39.—To a solution of bis(3,20-bisethylenedioxypregna-5,16-dien-21-yl) carbonate (50 mg) in methylene chloride (10 ml) and methanol (15 ml) was added 8% aqueous sulfuric acid (2 ml). The mixture was boiled until most of the methylene chloride was gone, then refluxed for an additional 90 min. The product, recovered after concentration *in vacuo* and methylene chloride extraction, crystallized from methanol as needles, mp 238–242°, in quantitative yield. A mixture melting point with **29** prepared by phosgenation of **25** was 240–244° and their ir spectra were identical.

Bis(3,11,20-trioxopregna-4,16-dien-21-yl) Carbonate (30) from 26.—Phosgenation of 21-hydroxypregna-4,16-diene-3,11,20-trione (68 mg, 0.2 mmol) under condition A and crystallization of the product from methanol gave 48 mg (68%) of needles: mp 171–173°; $[\alpha]_D$ +250°; λ_{max} 238 mμ (ε 48,500); ν_{max} 1760, 1272, and 786 (bisteroidal carbonate), 1670 (C-3 and C-20 ketones), 1619 (Δ^4), 1591 cm^{-1} (Δ^{16}).

Anal. Calcd for $C_{43}H_{50}O_9$: C, 72.65; H, 7.09. Found: C, 72.43; H, 6.91.

30 from 40.—Acid hydrolysis of bis(3,20-bisethylenedioxy-11-oxopregna-5,16-dien-21-yl) carbonate (50 mg) as in the preparation of **29** from **39** and crystallization from methanol furnished 35 mg (88%) of needles, mp 176–178°. The ir spectrum was identical with that of **30** prepared by phosgenation of **26** under condition A.

Registry No.—**1**, 64-85-7; **2**, 26987-64-4; **3a**, 39703-91-8; **3b**, 39703-92-9; **4**, 39833-00-6; **5**, 39833-01-7; **6**, 36675-01-1; **7**, 57-83-0; **8a**, 39833-03-9; **8b**, 39833-04-0; **9**, 72-23-1; **10**, 39833-05-1; **11a**, 39704-16-0; **11b**, 39704-17-1; **12**, 516-15-4; **13**, 13382-00-8; **14b**, 26437-02-5; **15b**, 26437-04-7; **16**, 5598-02-7; **17**, 39833-10-8; **18**, 39833-11-9; **19**, 39833-12-0; **20**, 39833-13-1; **21**, 39833-14-2; **22**, 39900-65-7; **23**, 39833-15-3; **24**, 39833-16-4; **25**, 39833-17-5; **26**, 39833-18-6; **27**, 39833-19-7; **28**, 39703-59-8; **29**, 39833-21-1; **30**, 39833-22-2; **31**, 39833-23-3; **32**, 39900-66-8; **33**, 39833-24-4; **34**, 39833-25-5; **35**, 39833-26-6; **36**, 39833-27-7; **37**, 39833-28-8; **38**, 39833-29-9; **39**, 39833-30-2; **40**, 39833-31-3; **41**, 36675-03-3; **42**, 36623-32-2; bis(17β-methyl-3,20-bisethylenedioxy-18-nor-17α-pregna-5,13(14)-dien-21-yl) carbonate, 39833-32-4.

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Reactions of α-Ketols and Other 21-Hydroxy Steroids with Phosgene. III. Dehydrohalogenation Products from 20-Chloro-20,21-cyclic Carbonates[1]

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Dehydrohalogenation of the cyclic chlorocarbonate mixture (**1a,b**) from 11-deoxycorticosterone either in hot pyridine or acetone–sodium iodide–triethylamine affords the $\Delta^{20,21}$-20,21-cyclic carbonate **2** and the trans and cis $\Delta^{17,20}$-20,21-cyclic carbonates **3** and **4**, respectively. Sequential treatment of the cis isomer **4** with sodium borohydride and chromic anhydride–pyridine provides the 20β,21-cyclic carbonate **5b**, whereas similar reaction of the trans isomer **3** gives the 20β-hydroxy-21-camylate **6b**. Definitive configurational assignments for **3** and **4** were made by their independent synthesis *via* dehydration with thionyl chloride in pyridine of 17-hydroxy-20,21-cyclic carbonates of known orientation at C-20. Dehydrohalogenation of the cyclic chlorocarbonate mixture (**19a,b**) from 11-dehydrocorticosterone also provides three unsaturated cyclic carbonates (**20**, **21**, and **22**). The geometric isomers from **19a,b** were also synthesized *via* 17-hydroxy-20,21-cyclic carbonates. It was also found that Δ^{16} compounds, which are minor products in the dehydration of hydroxy cyclic carbonates, can be obtained in good yield when 17-hydroxy-20,21-diacetates are substrates. Structural correlations among Δ^{16}-cyclic carbonates, Δ^{16}-diacetates, and Δ^{16}-α-ketols in both the 11-deoxy and 11-keto series were made *via* Δ^{16}-20-hydroxy-21-camylates.

In the preceding paper[2] we reported that novel 20-chloro-20,21-cyclic carbonates are generated in the reaction of 11-deoxy- and 11-dehydrocorticosterone in pyridine with excess phosgene in benzene (condition B). The chlorocarbonates from the former α-ketol could be obtained only as an epimeric mixture (**1a,b**, Scheme I), but the corresponding 11-ketones (**19a** and **19b**, Scheme II) were isolated in pure form. Preliminary experiments directed toward purification of the epimeric mixture **1a,b** showed that loss of hydrogen chloride occurs readily, and the resulting products appeared to be of sufficient interest to warrant a separate, detailed investigation of their formation and reactions. In the present paper we describe the isolation and identification of the dehydrohalogenation products both from cyclic chlorocarbonates **1a,b** and **19a,b** as well as their independent syntheses. In the course of these studies a number of C-20-epimeric Δ^{16}-20,21-diols and their derivatives were encountered. A description of their preparation and properties will also be presented.

As described earlier,[2] addition of either steroidal or nonsteroidal primary alcohols to a solution of **1a,b** in pyridine affords mixed carbonates in good yield. It

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(2) M. L. Lewbart, *J. Org. Chem.*, **38**, 2328 (1973).