mixture was then evaporated to give a free-running powder. This material was added to a dry column of silica gel (41 × 3.3 cm) so that the final size was 61 × 3.3 cm. The column was eluted with chloroform and 100-ml fractions were collected. At fraction 11 the solvent was changed to chloroform–methanol (9:1). Fractions 15–20, which were homogeneous as judged by tlc on SilicAR 7GF with ethyl acetate developer (detection with sulfuric acid), were evaporated to dryness. The syrupy residue was crystallized from ethanol–heptane to yield 6.36 g (88%) of white product, mp 179–181°. This material was recrystallized from ethanol–heptane to give pure product: mp 180–181°; λ_{max}^{KBr} 1680–1800 cm^{-1} (C=O of cyanuric acid); pmr (DMSO-d_6) δ 1.32 (s, 3, CCH_3), 1.52 (s, 3, CCH_3), 3.54 ("d," 2, "J" = 6.5 cps, 5′ CH_2OH), 3.80–4.18 (m, 1, 4′ H), 4.54–4.93 (m, 2, 3′ H and 5′ CH_2OH), 5.17 (d, 1, $J_{2',3'}$ = 6.0 cps, 2′ H), 6.18 (s, 1, $J_{1',2'}$ <1 cps, 1′ H), and 11.84 (broad, s, 2, NH).

Anal. Calcd for $C_{11}H_{15}N_3O_7$: C, 43.85; H, 5.02; N, 13.95. Found: C, 44.21; H, 5.45; N, 14.20.

1-(2,3-*O*-Isopropylidene-5-methylsulfonyl-β-D-ribofuranosyl)-cyanuric Acid.—To a stirred solution of 1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)cyanuric acid (6.32 g) in dry pyridine (50 ml) at 0° was added dropwise methylsulfonyl chloride (1.80 ml) and the resulting solution was sealed and stored at 0° for 36 hr. Absolute ethanol (a few drops) was added and the solution was left overnight at 0°. The solution was evaporated to dryness and the residue was coevaporated with toluene. The dried (oil pump vacuum) residue was dissolved in methanol and silica gel was added. The mixture was evaporated to give a free-running powder which was added to a column (51 × 3.5 cm) of silica gel so that the final dimensions were 72 × 3.5 cm. Elution was started with chloroform. Fractions (200 ml each) were collected and the fractionation was monitored by tlc on SilicAR 7GF with ethyl acetate–chloroform (7:3) as developer (detection by sulfuric acid). At fraction 9 the solvent was changed to chloroform–ethyl acetate (4:1) and at fraction 14 to ethyl acetate. Fractions 16–19, which were of 100-ml volume and which contained a single component, were pooled and evaporated to a foam. Crystallization from ethyl acetate–heptane yielded 7.06 g (89%) of white crystals, mp 194–196°. These crystals were dissolved in methanol and the solution was decolorized. After solvent removal, the product was crystallized from ethanol–heptane to give pure material: mp 195–197°; ν_{max}^{KBr} 1710–1760 cm^{-1}; pmr (DMSO-d_6) 1.33 (s, 3, CCH_3), 1.52 (s, 3, CCH_3), 3.20 (s, 1, 5′ CH_3SO_2), 4.10–4.60 [m, 3, 5′ CH_2O (s) at 4.36 overlapped by 4′ H], 4.74–4.98 (m, 1, 3′ H), 5.21 (d, 1, $J_{2',3'}$ = 7.0 cps, 2′ H), 6.14 (s, 1, $J_{1',2'}$ <1 cps, 1′ H), and 11.66 (s, 2, NH).

Anal. Calcd for $C_{12}H_{17}N_3O_9S$: C, 37.98; H, 4.52; N, 11.08. Found: C, 37.88; H, 4.42; N, 11.04.

Registry No.—I, 320-67-2; III, 2353-33-5; IV, 22432-95-7; V, 22432-96-8; VI, 22432-97-9; VII, 22432-98-0; 1-(3,5-di-*O*-acetyl-2-deoxy-α,β-D-ribofuranosyl)-5-azacytosine, 22432-93-5; 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)cyanuric acid, 22432-99-1; 1-(2,3,5-tri-*O*-acetyl-α-D-arabinofuranosyl)-5-azacytosine, 22433-00-7; 1-(2,3-isopropylidene-β-D-ribofuranosyl)cyanuric acid, 22433-01-8; 1-(2,3-*O*-isopropylidene-5-methylsulfonyl-β-D-ribofuranosyl)cyanuric acid, 22433-02-9.

Synthesis of 21-Hydroxymethylprogesterone

A. F. HIRSCH[1] AND G. I. FUJIMOTO

Albert Einstein College of Medicine, Yeshiva University, Bronx, New York 10461

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The synthesis of 21-hydroxymethylprogesterone was accomplished by two pathways, from progesterone and from 3β-acetoxy-5-pregnen-20-one. The preferred method involved the formylation and subsequent borohydride reduction of the 3-monoketal of progesterone. This diol was subsequently tritylated, oxidized, and hydrolyzed to yield 21-hydroxymethylprogesterone.

The C-17 side chains of the progestational and adrenocortical steroid hormones may be compared with the lowest members of the deoxy sugar and sugar series, respectively. Elongation of these side chains by addition of hydroxymethyl groups would yield homologs of the steroid-substituted carbohydrates. The higher hydroxymethyl homologs of progesterone and cortisol would have side chains which may be pictured as 1-substituted deoxy ketoses and 1-substituted ketoses, respectively. We wish to report the synthesis of 21-hydroxymethylprogesterone (**7a**), our initial objective in these studies.

A simple, direct method has been reported for the synthesis of 21-hydroxymethylcortisol by condensation of cortisol with formaldehyde.[2] When we attempted this method with pregnenolone and formaldehyde, we recovered only starting steroid. Our further studies with this method will be the subject of a separate paper. We did not obtain monohydroxymethylation in the desired position.

Very few primary aliphatic α-unsubstituted β-hydroxy ketones have been reported in the literature.[3] We presumed that 21-hydroxymethylprogesterone would be quite labile and that synthesis by indirect methods would be very sensitive to manipulations involved in protecting the other functional groups in the molecule. This did not prove to be the case.

The addition of the hydroxymethyl group on C-21 was accomplished by condensation of the 17β-acetyl group of pregnenolone acetate (**1**) with formate ester[4] followed by reduction with borohydride to the triol **2a** in the reaction medium (Scheme I). A number of routes were considered in order to utilize this condensation reaction for the synthesis of 21-hydroxymethylprogesterone. That the formate condensation occurs on C-21 has been demonstrated by Hirai, *et al.*,[5] as well as from evidence below.

One approach was to form the 20,21a-acetonide derivative[6] of the triol **2a** in order to oxidize selectively the Δ^5-3β-hydroxyl to the Δ^4-3-ketone by the Oppenauer method. Hydrolysis of the acetonide **4** yielded the diol ketone **5a**. The overall yield of this method to this point was so low that we turned to other approaches. An attempt to shortcut this pathway by tritylation of

(1) (a) Senior Postdoctoral Fellow, 1965–1967, supported by Grant 5 TU-MH6418, National Institutes of Health.

(2) S. Noguchi and K. Morita, *Chem. Pharm. Bull.* (Tokyo), **11**, 1235 (1963).

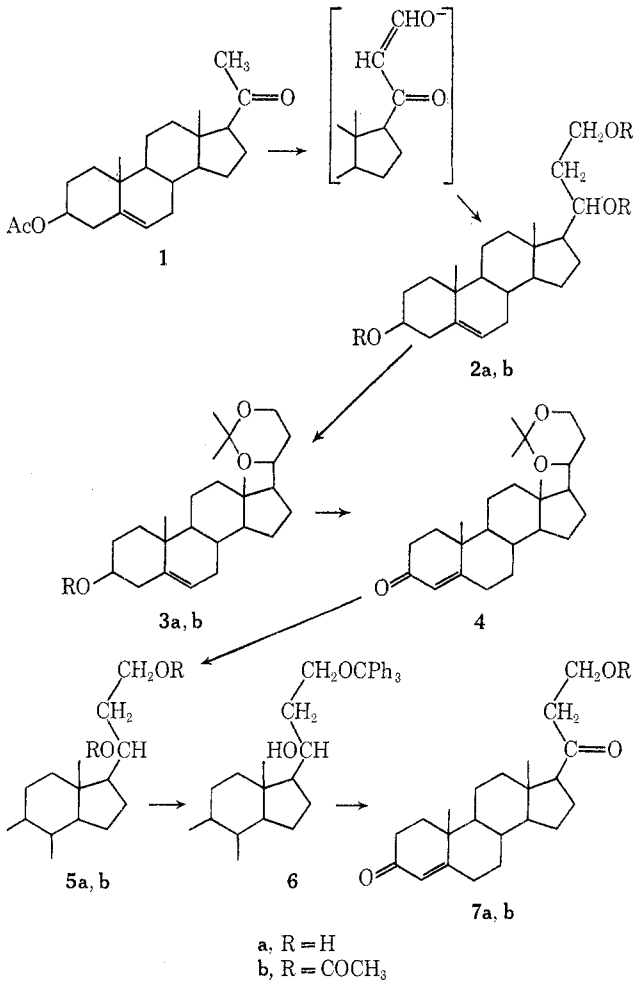
(3) See, *e.g.*, T. White and R. N. Howard, *J. Chem. Soc.*, 25 (1943), and the patent literature for 1-hydroxybutan-3-one.

(4) L. Ruzicka, U. S. Patent 2,398,861 (1946); W. Bockmühl, G. Ehrhart, and H. Ruschig, German Patent 871,451 (1953); N. J. Doorenbos and L. Milewich, *J. Org. Chem.*, **31**, 3193 (1966).

(5) S. Hirai, R. G. Harvey, and E. V. Jensen, *Tetrahedron*, **22**, 1625 (1966).

(6) M. Tanabe and B. Bigley, *J. Amer. Chem. Soc.*, **83**, 756 (1961); A. Hampton, J. C. Fratantoni, P. M. Carroll, and S. Wang, *ibid.*, **87**, 5481 (1965).

SCHEME I



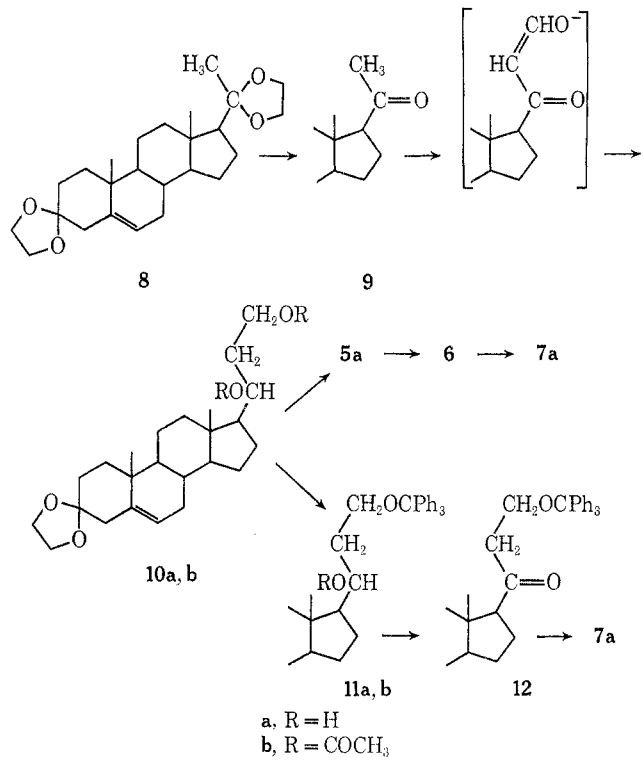
the triol **2a** followed by oxidation of both the C-3 and C-20 hydroxyls simultaneously was unsuccessful.

The more fruitful method was to start with progesterone and mask the 3-ketone with an ethylene ketal derivative **9** prepared by selective hydrolysis of the 3,20-bisketal of progesterone (**8**) (Scheme II). Condensation of the 3-monoketal **9** with isoamyl formate followed by borohydride reduction yielded the 20,21a-dihydroxy 3-ethylene ketal **10a**. On hydrolysis this yielded the same diol ketone **5a** as the first method. The configuration of the 20-hydroxyl is presumed to be β, since sodium borohydride reduction of the 20-ketones yields almost exclusively the 20β-ols.[7] From nmr spectral data the characteristic upfield shift for the C-18 methyl of 0.11 ppm is observed following acetylation of the 20β,21a-diol 3-ketone **5a** to the 20β,21a-diacetoxy 3-ketone **5b**, substantiating the 20β configuration for the hydroxyl group.[8] There is indication of some 20α-hydroxyl formation from the minor product which was separated on tlc but not characterized further. By protecting the C-21a primary hydroxyl of **5a** by tritylation, we selectively oxidized the C-20 hydroxyl with chromic acid–pyridine to the trityl diketone, which was not isolated. Mild hydrolysis of the trityl group gave the desired 21-hydroxymethylprogesterone (**7a**) in 59% yield from **10a**.

(7) See, *e.g.*, L. F. Fieser and M. Fieser," Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p 568.

(8) See C. H. Robinson and P. Hofer, *Chem. Ind.* (London), 377 (1966); H. Lee and M. E. Wolff, *J. Org. Chem.*, **32**, 192 (1967).

SCHEME II



It was surprising that no other products were observed on tlc. This was an indication of the relative stability of this β-hydroxy ketone.

The above method was simplified by removing the ketal group simultaneously with the trityl group in the synthesis. The 20β,21a-diol 3-ketal **10a** was tritylated, then oxidized at C-20 to the 21a-trityl 20-ketone 3-ketal **12**. Mild acid hydrolysis removed both the trityl and the ketal to yield 21-hydroxymethylprogesterone. This method gave the best overall yields (63% from **10a**).

The difficulties anticipated in the removal of protective groups in the β-hydroxy keto steroids were not realized. In fact, the 21a-hydroxy 20-keto steroid appears to be much more stable than anticipated and to be quite resistant to the usual dehydration procedures. Neither mild acid nor alkali appears to alter this structure.

Experimental Section

Analyses were determined by Spang Microanalytical Laboratory, Ann Arbor, Mich. Ir spectra were recorded with a Perkin-Elmer Model 21 spectrophotometer; nmr spectra with a Varian Model A-60 spectrometer in $CDCl_3$ with $SiMe_4$ as internal standard; and ORD spectra with a Cary Model 60 spectropolarimeter in dioxane unless otherwise stated. Melting points were determined on a Kofler hot stage. For tlc, silica gel GF was used, and, for silica gel columns, SilicAR cc-7, 100–200 mesh, was used.

21-Methyl-5-pregnene-3β,20β,21a-triol (2a).[9]—A solution of 30 g (84 mmol) of pregnenolone acetate (**1**) in 1.3 l. of anhydrous benzene was distilled to remove about 100 ml of a benzene azeotrope. To the cooled solution, under nitrogen, were added with stirring 10.92 g of sodium hydride (55% in oil) and 33.3 ml of freshly distilled isoamyl formate. The mixture was refluxed for 12 hr and cooled, and to it 9.5 g of sodium borohydride and 500 ml of methanol were added. The mixture was stirred overnight, diluted with 150 ml of water, neutralized with sulfuric acid, and concentrated *in vacuo*. The solid residue was washed

(9) We wish to acknowledge the generous assistance of Mr. A. S. Tarendash in the preparation of this substance.

with water, dried *in vacuo*, and crystallized from acetone, affording 9.8 g (33.6%) of product **2a**, which was sufficiently pure for the subsequent steps. A sample was recrystallized from acetone, mp 183–185° (softening at 178°), ir (KBr) 3.01 μ (OH).

Anal. Calcd for $C_{22}H_{36}O_3 \cdot {}^1/_2H_2O$: C, 73.96; H, 10.43. Found: C, 73.88; H, 10.21.

The triol **2a** was acetylated to the triacetate **2b** in 66% yield, mp 139–143.5° (softening at 137°), ir (CS_2) 5.74 (ester C=O) and 8.10 μ (ester COC).

Anal. Calcd for $C_{28}H_{42}O_6$: C, 70.86; H, 8.92. Found: C, 70.78; H, 8.77.

20β,21a-Isopropylidenedioxy-21-methyl-5-pregnen-3β-ol (3a). Method A.—To a solution of 383 mg (1.1 mmol) of triol **2a** in 3 ml of dimethylformamide were added 5 ml of 2,2-dimethoxypropane and 10 mg of *p*-toluenesulfonic acid. The solution was stirred for 75 min, neutralized with dilute sodium bicarbonate, and extracted with benzene. The extract was washed with water, dried ($MgSO_4$), and concentrated. The residue (403 mg) was chromatographed on 20 g of alumina (Merck) and the methylene chloride eluate gave 302 mg of crude product, which on crystallization from acetone yielded 185 mg (48%) of **3a**, mp 190–192° subl, ir (CS_2) 2.82 (OH) and 7.29 μ (acetonide).

Anal. Calcd for $C_{25}H_{40}O_3$: C, 77.27; H, 10.38. Found: C, 77.11; H, 10.27.

Method B.—A suspension of 3.48 g (10 mmol) of **2a**, 400 ml of acetone, 15 ml of 2,2-dimethoxypropane, and 340 mg of di(*p*-nitrophenyl) phosphate was stirred for 5 hr (dissolution occurring in 20 min) at room temperature. After addition of 200 mg of sodium bicarbonate, the solution was concentrated *in vacuo*. The residue was taken up in ether, washed with water, dried ($MgSO_4$), and concentrated. After crystallization from methylene chloride or acetone, 2.85 g (73%) of **3a** was obtained, mp 191–193° and identical in ir spectrum and chromatographic mobility with product from method A.

The acetate **3b** was prepared in quantitative yield from **3a**: mp 188–193° subl; ir (CS_2) 5.77 (ester C=O), 7.29 (acetonide), and 8.09 μ (ester COC); nmr δ 5.44 (br, 1, C-6), 3.84 (m, 2, C-21a), 2.03 (s, 3, CH_3CO), 1.47 (s, 3, acetonide CH_3 axial), 1.35 (s, 3, CH_3 equatorial), 1.02 (s, 3, C-19), and 0.73 (s, 3, C-18).

Anal. Calcd for $C_{27}H_{42}O_4$: C, 75.31; H· 9.83. Found: C, 75.33; H, 9.91.

Oppenauer Oxidation of 3a.—A solution of 176 mg (0.45 mmol) of **3a**, 30 ml of toluene, and 5 ml of cyclohexanone (freshly distilled reagents) was distilled to remove *ca.* 3 ml of toluene. After addition of 200 mg of aluminum isopropoxide, the solution was refluxed for 2 hr and allowed to stand overnight. A yellow, gum residue was obtained after concentration *in vacuo*. To this was added 70 ml of 10% Rochelle salt solution and 150 ml of ether. The ethereal solution was washed with water, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed on silica gel and eluted with 1% acetone in benzene. The product obtained was crystallized from acetone, yielding 17.6 mg (10%) of chromatographically pure **4**: mp 183–186° subl; ir (CS_2) 5.96 (C=O) and 7.28 μ (acetonide); nmr δ 5.79 (br, 1, C-4), 1.49 (s, 3, acetonide, CH_3 axial), 1.36 (s, 3, CH_3 equatorial), 1.21 (C-19), and 0.73 (C-18).

Anal. Calcd for $C_{25}H_{38}O_3$: C, 77.68; H, 9.91. Found: C, 77.58; H, 9.94.

20β,21a-Dihydroxy-21-methyl-4-pregnen-3-one (5a).—A solution of 23.4 mg (0.061 mmol) of acetonide **4** in 1 ml of 90% acetic acid was allowed to stand at room temperature for 3 hr. The process of concentrating *in vacuo*, adding benzene, and reconcentrating was repeated three times. The product, obtained in quantitative yield, was crystallized from acetone, mp 198–201°; when compared with **5a** from series II there was no depression in melting point on admixture and ir spectra were identical.

21-Hydroxymethylprogesterone (7a) Prepared from Diol Ketone 5a.—A solution of 1.328 g of diol ketone **5a** in 20 ml of pyridine (freshly distilled) was partially distilled and replenished with pyridine twice. After 1.175 g of trityl chloride was added, the solution was allowed to stand for 3 days. The trityl hydroxy ketone **6** proved to be very deliquescent and was not characterized further. The pyridine solution of **6** was added to a solution of 500 mg of CrO_3 in 20 ml of pyridine. Two more portions of 500 mg of CrO_3 in pyridine were added over a period of 7 days until the reaction was complete according to tlc. After 10 ml of methanol was added, the solution was concentrated *in vacuo* and extracted with ether. The extract was filtered, washed with water, concentrated, and hydrolyzed with 20 ml of 70% acetic acid over 4 days. The residue was concentrated *in vacuo*, extracted with ether, washed, dried, and chromatographed on 45 g of silica gel. From the benzene–acetone (9:1) fraction was obtained 911 mg (69%) of **7a**, crystallized from acetone, mp 138–139°; when compared with **7a** prepared from **10a**, there was no depression in melting point on admixture and ir spectra were identical.

5-Pregnene-3,20-dione 3-Ethylene Ketal (9).[10]—To 100 mg (0.25 mmol) of progesterone bisethylene ketal (**8**)[11] in 25 ml of water-saturated benzene was added 2.5 ml of 0.01 *M* *p*-toluenesulfonic acid in ether. After the mixture was stirred for 70 min at room temperature, 50 ml of benzene and 50 ml of 10% $NaHCO_3$ were added. The organic phase was washed well with water, dried, (K_2CO_3), and concentrated, yielding 86 mg (96%) of a product sufficiently pure for the subsequent reactions. Crystallization from methanol and then from acetone gave **9**, mp 174.5–176.5° (lit. mp 180–181°,[12a] 178–180°[12b]).

20β,21a-Dihydroxy-21-methyl-5-pregnen-3-one 3-Ethylene Ketal (10a).—A solution of 4.89 g (13.62 mmol) of the 3-monoethylene ketal (**9**) of progesterone in 550 ml of dry benzene was distilled to remove *ca.* 50 ml of a benzene azeotrope. To the cooled solution under a nitrogen atmosphere was added with stirring 1.82 g of sodium hydride (55% in oil) and 5.5 ml of freshly distilled isoamyl formate. The mixture was refluxed for 4 hr and cooled, and 3.6 g of sodium borohydride and 100 ml of methanol were added and the resultant mixture was stirred overnight. After the mixture was concentrated under reduced pressure and 600 ml of water was added, a suspension was formed which was extracted thoroughly with ether until no solid remained. The combined ether solution was washed with water, dried ($MgSO_4$), and concentrated. In later work methylene chloride was used for the extraction because of greater solubilizing properties. The crude product was crystallized from acetone, affording 5.19 g (97.4%) of product sufficiently homogeneous to use in subsequent steps. A sample for analysis was prepared by chromatography on alumina (Merck) from the fraction eluted with methanol–methylene chloride (1:1). A small amount of what is probably the 20α isomer of **10a** was separated by chromatography. Two recrystallizations of the major fraction (90%) from acetone yielded **10a**: mp 196–199.5° subl; ir ($CHCl_3$) 2.80 (sh) and 2.88 μ (OH); nmr δ 5.4 (br, 1, C-6), 3.95 (ketal), 3.88 (t, 2, J = 6 cps, C-21a), 1.04 (C-19), and 0.79 (C-18).

Anal. Calcd for $C_{24}H_{38}O_4$: C, 73.81; H, 9.81. Found: C, 74.02; H, 9.80.

Acetylation of the diol ketal **10a** gave a quantitative yield of the diacetate **10b**: mp 164–168°; ir (CS_2) 5.74 (ester C=O), 8.06, and 8.16 μ (ester COC); nmr δ 5.37 (br, 1, C-6), 5.07 (br, 1, C-20), 4.11 (t, 2, J = 7 cps, C-21a), 3.96 (ketal), 2.05 (acetates), 1.02 (C-19), and 0.69 (C-18).

Anal. Calcd for $C_{28}H_{42}O_6$: C, 70.86; H, 8.92. Found: C, 70.76; H, 8.80.

Hydrolysis of Ketal 10a.—A solution of 700 mg of ketal **10a** in 100 ml of 80% acetic acid, after standing for 24 hr at room temperature, was diluted with two 100-ml portions of water and extracted thoroughly with methylene chloride. The extract was washed well with Na_2CO_3 and water, concentrated to dryness *in vacuo*, and crystallized from acetone. Three crops yielded 527 mg (85%). On chromatography on Woelm neutral alumina (activity I), the CH_2Cl_2–MeOH (9:1) fraction gave a nearly quantitative yield of the diol ketone **5a**, recrystallized twice from acetone as needles: mp 203.5–204.5°; ir ($CHCl_3$) 2.88 (OH), 6.02 (C=O), and 6.20 μ (C=C); nmr δ 5.75 (br, 1, C-4), 3.88 (t, 2, J = 5 cps, C-21a), 2.76 (OH), 2.29 (C-21), 1.2 (C-19), and 0.83 (C-18); ORD (*c* 0.056) $[\Phi]_{589}$ +285°, $[\Phi]_{420-405}$ +525° (broad peak), $[\Phi]_{364}$ −453°, $[\Phi]_{357}$ −262°, $[\Phi]_{350}$ −755°, $[\Phi]_{336}$ + 1244° (sh), $[\Phi]_{322}$ +3480° (sh), $[\Phi]_{308}$ +5816° (sh), and $[\Phi]_{275}$ +8540°.

Anal. Calcd for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.45; H, 9.61.

The diacetate **5b** was prepared in the usual way: mp 122–126°; ir (CS_2) 5.74, 8.09, and 8.16 μ (ester C=O, COC); nmr

(10) This procedure is a modification of the method of J. Schmidlin and A. Wettstein, *Helv. Chim. Acta*, **45**, 331 (1962).

(11) W. S. Allen, S. Bernstein, and R. Littell, *J. Amer. Chem. Soc.*, **76**, 6116 (1954).

(12) (a) F. Sondheimer, M. Velasco, and G. Rosenkranz, *ibid.*, **77**, 192 (1955); (b) A. Bowers, L. C. Ibanez, and H. J. Ringold, *Tetrahedron*, **7**, 138 (1959).

δ 5.75 (br, 1, C-4), 4.11 (t, 2, J = 7 cps, C-21a), 2.29 (t, 2, J = 7 cps, C-21), 2.05 (acetates), 1.19 (C-19), and 0.72 (C-18).

Anal. Calcd for $C_{26}H_{38}O_5$: C, 72.53; H, 8.90. Found: C, 72.65; H, 9.09.

Tritylation of 20β,21a-dihydroxy-21-methyl-5-pregnen-3-one 3-Ethylene Ketal (10a).—A solution of 4.22 g (10.8 mmol) of diol ketal **10a** in 75 ml of dry pyridine was partially distilled *in vacuo* and replenished with pyridine to a volume of 100 ml. To this was added 3.47 g of freshly crystallized trityl chloride and the solution was allowed to stand for 40 hr. Another 0.5 g of trityl chloride was added and 24 hr later no starting material remained according to tlc [acetone–benzene (1:4)]. The pyridine was removed *in vacuo* and the addition and distillation of benzene *in vacuo* was repeated three times. The residue was taken up in 150 ml of methylene chloride, washed with 5% $NaHCO_3$ solution and water, dried ($MgSO_4$), and concentrated to dryness. After crystallizing from acetone, 4.82 g of **11a** was obtained in two crops, mp 187–191°. The total yield of 6.0 g (88.3%) included a third crop of crystals, mp 179–183°. A sample was recrystallized from acetone for analysis: mp 188–191°; ir (CS_2) 2.86 (OH), 3.30, 3.33, 13.48, and 14.23 μ (aryl); nmr δ 7.23–7.53 (trityl), 5.4 (broad, 1, C-6), 3.95 (ketal), 3.35 (t, 2, J = 6 cps, C-21a), 1.05 (C-19), and 0.78 (C-18).

Anal. Calcd for $C_{43}H_{52}O_4$: C, 81.61; H, 8.28. Found: C, 81.63; H, 8.18.

The acetate **11b** was prepared from **11a** in quantitative yield and crystallized from acetone as colorless needles: mp 193–194°; ir (CS_2) 3.30, 3.34, 13.47, and 14.23 (aryl), 5.76 (ester C=O), and 8.10 μ (ester COC); nmr δ 7.2–7.5 (trityl), 5.36 (broad, 1, C-6), 4.95 (broad, 1, C-20), 3.93 (ketal), 3.12 (t, 2, C-21a), 1.84 (acetate),[13] 1.01 (C-19), and 0.64 (C-18).

Anal. Calcd for $C_{45}H_{54}O_5$: C, 80.08; H, 8.06. Found: C, 80.09; H, 8.12.

Chromium Trioxide Oxidation of 11a.—A solution of 2.26 g (3.58 mmol) of hydroxy trityl ketal **11a** in 40 ml of dry pyridine was added dropwise to a solution of 1.41 g (14.1 mmol) of chromium trioxide in 30 ml of dry pyridine and allowed to stand overnight at room temperature. After 300 ml of ether and 10 ml of methanol were added, the precipitate formed was filtered and washed with ether. The combined ether solution was washed with water and dried, and the solvent was removed *in vacuo*. The product solidified when treated with acetone–cold methanol and weighed 2.06 g (91%). This was sufficiently pure for the next step. Various attempts to prepare an analytical sample failed. From silica gel chromatography a homogeneous substance **12** was obtained from the benzene fraction: mp 78.5–81.5°; ir (CS_2) 3.29, 3.32, 13.47, and 14.22 (aryl), and 5.86 μ (20 C=O); nmr δ 7.2–7.6 (trityl), 5.4 (br, 1, C-6), 3.96 (ketal), 3.44 (t, 2, J = 6 cps, C-21a), 2.62 (t, 2, J = 6 cps, C-21), 1.03 (C-19), and 0.63 (C-18).

21-Hydroxymethylprogesterone (7a).—Hydrolysis of 1.72 g (2.73 mmol) of 21-trityloxymethylprogesterone 3-ethylene ketal (**12**) in 100 ml of 80% acetic acid was complete after the solution had been shaken for 17 hr at room temperature. After 100 ml of water was added, the solution was extracted with ether and the organic extract was washed with dilute Na_2CO_3 and water, dried ($MgSO_4$), and concentrated *in vacuo* to a yellowish gum. The residue was chromatographed on silica gel, and the fraction eluted with acetone–benzene (1:4) yielded 726 mg (78%) of **7a**, which was crystallized from acetone: mp 140.5–141.5°; uv max (MeOH) 241 mμ (ε 17,800); ir (CS_2) 2.82 (OH), 5.90 (20 C=O), and 5.96 μ (3 C=O); nmr δ 5.74 (br, 1, C-4), 3.85 (t, 2, J = 5 cps, C-21a), 2.62 (t, 2, J = 5 cps, C-21), 1.19 (C-19), and 0.69 (C-18); ORD (c 0.0527) $[\Phi]_{589}$ + 550°, $[\Phi]_{365}$ +1540°, $[\Phi]_{356}$ +2000°, $[\Phi]_{351}$ +1870°, $[\Phi]_{312}$ +15,200°, $[\Phi]_{273}$ +780°.

Anal. Calcd for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 76.54; H, 9.57.

Acetylation of **7a** resulted in a quantitative yield of the acetate **7b**, which crystallized from acetone in orthorhombic prisms: mp 129–129.5°; ir (CS_2) 5.73 (ester C=O) and 8.14 (ester COC), 5.86 (20 C=O), and 5.96 μ (3 C=O); nmr δ 5.78 (br, 1, C-4), 4.38 (t, 2, J = 6 cps, C-21a), 2.72 (t, 2, J = 6 cps, C-21), 2.04 (acetate), 1.20 (C-19), and 0.71 (C-18).

Anal. Calcd for $C_{24}H_{34}O_4$: C, 74.58; H, 8.87. Found: C, 74.39; H, 8.75.

Registry No.—**2a**, 22486-07-3; **2b**, 22528-31-0; **3a**, 22486-08-4; **3b**, 22486-09-5; **4**, 22486-10-8; **5a**, 22486-11-9; **5b**, 22486-12-0; **7a**, 22486-13-1; **7b**, 22486-15-3; **10a**, 22486-16-4; **10b**, 22485-90-1; **11a**, 22485-91-2; **11b**, 22485-92-3; **12**, 22528-29-6.

(13) The acetate protons shifted upfield by 0.20 ppm in the presence of a trityl group. See, *e.g.*, D. Horton, J. B. Hughes, J. S. Jewell, K. D. Philips, and W. N. Turner, *J. Org. Chem.*, **32**, 1073 (1967).

Photochemistry of 5-Norbornenylacetone and 5-Norbornenylacetaldehyde

R. R. SAUERS AND K. W. KELLY

School of Chemistry, Rutgers University, New Brunswick, New Jersey 08903

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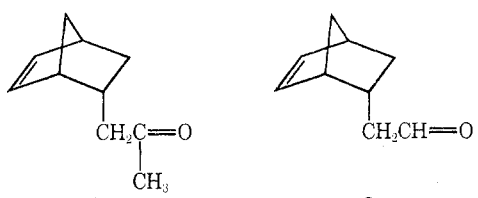
Irradiation of the δ,ε-unsaturated carbonyl compounds **1** and **2** led to mixtures of oxetanes as the major photoproducts.

As part of a broad study of the photochemical behavior of unsaturated polycyclic ketones,[1] it was of interest to examine the two norbornene systems **1** and **2**. It was hoped that studies of these systems would be informative as to the intramolecular modes of interaction of the excited carbonyl groups with the double bond. More specifically, for example, one has the possibility of intramolecular energy transfer[2] from the triplet state of the carbonyl group of **1** (E_T = 80–82 kcal/mol[3]) to the norbornene double bond ($E_T \cong$ 72 kcal/mol[4]). On the other hand, triplet transfer from the aldehyde function of **2** ($E_T \cong$ 69 kcal/mol[5]) would be expected to be considerably less efficient. Substantive product differences in the two cases would serve as a basis for interpretations as to the nature of the transfer process. Lastly, our interest in these systems was enhanced by the intriguing chemical possibilities, *e.g.*, Norrish Type II cleavage or cyclobutanol formation, which might



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