ferent chemical shifts and additional splitting, whereas the α protons would be equivalent in the ortho ester. What was actually observed was a chemical shift difference and complex splitting of the α protons.

Table IV lists the principal infrared peaks of the alkyl 2,2-dialkoxypropanoates that are characteristic and identifiable. Broad absorption owing to C—O stretching was observed in the 8.5- to 9.0-μ region. The broadness was probably the result of overlap of the ketal and ester C—O stretching bands. The absorption in the 13.1-μ region was present in all of the derivatives and could be the most useful in identifying these ketal esters. It has been tentatively assigned to ester stretching.

TABLE IV
CHARACTERISTIC INFRARED BANDS (μ)

Derivative	C=O stretch[a]	Ester[a]	C—O stretch, ester and ketal (very broad)[a,b]	Ester[c]
Methyl	5.67	7.73	8.20–9.00	13.11
Ethyl	5.70	7.77	8.35–9.00	13.14
n-Propyl	5.72	7.80	8.50–9.00	13.14
Allyl	5.72	7.81	8.48–9.02	13.10
n-Butyl	5.70	7.80	8.50–9.00	13.10
Isobutyl	5.70	7.80	8.52–8.98	13.10
n-Pentyl	5.75	7.84	8.60–9.00	13.16
Isopentyl	5.72	7.80	8.60–9.00	13.17

[a] Strong. [b] Occasionally resolved slightly into more than one band. [c] Medium to weak; tentative assignment.

Experimental Section[6]

Preparation of 2,2-Dialkoxypropanes.—The dialkoxypropanes were prepared according to the method of Lorette and Howard.[2] Redistilled Eastman 2,2-dimethoxypropane and alcohols were used. Three new 2,2-dialkoxypropanes were prepared.

2,2-Diisobutoxypropane had bp 56–57° (4 mm), d^{25}_4 0.8205, $n^{25}D$ 1.4036. *Anal.* Calcd for $C_{11}H_{24}O_2$: C, 70.16; H, 12.85. Found: C, 70.11; H, 12.50.

2,2-Di-*n*-pentoxypropane had bp 79–80° (4 mm), d^{25}_4 0.8337, $n^{25}D$ 1.4170. *Anal.* Calcd for $C_{13}H_{28}O_2$: C, 72.17; H, 13.05. Found: C, 72.20; H, 13.11.

2,2-Diisopentoxypropane had bp 71–72° (4 mm), d^{25}_4 0.8259, $n^{25}D$ 1.4136. *Anal.* Calcd for $C_{13}H_{28}O_2$: C, 72.17; H, 13.05. Found: C, 71.71; H, 12.71.

Preparation of Alkyl 2,2-Dialkoxypropanoates.—Eastman pyruvic acid was carefully distilled under vacuum, and an anhydrous fraction was taken for further work. The quantities of reactants, solvent, and catalyst shown in Table I were combined in a 250-ml, round-bottom flask. One drop of methyl sulfoxide was added[7] and the solution was refluxed. Periodically samples were removed and analyzed on an Aerograph Model 90 CS gas chromatograph with the use of a 5 ft × 0.25 in. 8% Dow 702 silicone on 60–80 mesh Celite column. When gas chromatography showed reaction was complete, the mixture was distilled slowly until approximately 25 ml was collected. A 10% sodium alkoxide solution was added until the reaction mixture was alkaline to wet litmus. Distillation was continued at reduced pressure and the alkyl 2,2-dialkoxypropanoate was collected over the boiling point range shown in Table II. The product was further purified by preparative gas chromatography with the use of the instrument mentioned above and a 5 ft × 0.5 in. 20% SE30 silicone on 60–80 mesh Celite column.

Nmr and Infrared.—Nmr spectra were measured on a Varian Model A-60 instrument.[8] The infrared spectra were measured on a Perkin-Elmer Model 137 spectrophotometer.

(6) Microanalyses by Drs. G. Weiler and F. B. Strauss, Microanalytical Laboratory, Oxford, England.

(7) P. G. Simmonds and A. Zlatkis, *Anal. Chem.*, **37**, 302 (1965).

(8) The authors wish to thank Dr. J. R. Vercellotti for obtaining the spectra.

Registry No.—2,2-Diisobutoxypropane, 10076-56-9; 2,2-di-*n*-pentoxypropane, 10076-57-0; 2,2-diisopentoxypropane, 10294-76-5.

Preparation and Deamination of 6β-Amino-17β,19-dihydroxy-3α,5α-cycloandrostane

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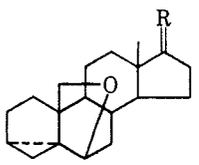
Received December 1, 1966

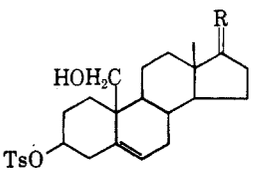
Kinetically controlled solvolyses of steroid Δ^5-3β-*p*-toluenesulfonates[1] and deaminations of steroid Δ^5-3β-amines[2] lead to 6β-substituted 3α,5α-cyclo steroids[3] *via* homoallylic cation intermediates. It has been shown that the presence of a hydroxyl group at C_{19}, which might conceivably effect intramolecular solvation of the β face of the homoallylic cation at C_6, does not alter the stereochemistry of kinetically controlled hydrolysis.[4]

The present study was undertaken to determine the effect of a 19-hydroxyl group on the stereochemistry of reaction at C_6 of a steroid 19-hydroxy-3α,5α-cyclo-6-carbinyl cation generated under both ammonolysis and deamination conditions.

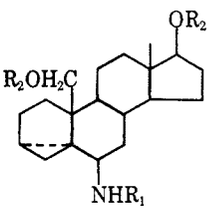
Thermodynamically controlled, acid-catalyzed solvolyses of 6β,19-oxido-3α,5α-cyclo steroids have been found to give rise to 19-hydroxy-Δ^5-3β-substituted steroids in which the 3β substituent is derived from the conjugate base of the solvent.[5] In the present work, brief treatment of the 6β,19-oxido-3α,5α-cyclo steroids Ia[5a] and Ib with excess *p*-toluenesulfonic acid in an-



Ia, R = O
b, R = 17β-OH and 17α-H



IIa, R = O
b, R = 17β-OH and 17α-H



IIIa, $R_1 = R_2 = H$
b, $R_1 = R_2 = COCH_3$
c, $R_1 = COCH_3$; $R_2 = H$

(1) N. L. Wendler in "Molecular Rearrangements," Part 2, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p 1075.

(2) J. Tadanier and W. Cole, *J. Org. Chem.*, **27**, 4615 (1962).

(3) An exception has been noted by L. A. Freiberg, *ibid.*, **30**, 2476 (1965), who found that both 3α,5α-cyclo-6α and -6β azides were formed on treatment of cholesteryl *p*-toluenesulfonate with sodium azide in several solvent systems.

(4) R. M. Moriarty and T. D. J. D'Silva, *Tetrahedron*, **21**, 547 (1965).

(5) (a) K. Tanabe, R. Takasaki, K. Sakai, R. Hayashi, and Y. Morisawa, *Chem. Pharm. Bull.* (Tokyo), **10**, 1126 (1962). (b) J. Tadanier, *J. Org. Chem.*, **28**, 1744 (1963). (c) R. M. Moriarty and T. D. J. D'Silva, *ibid.*, **28**, 2445 (1963).

TABLE I[a,b]

A. Δ^5-3β-*p*-Toluenesulfonates

Compd	C_3-H	C_{13}-Methyl	17α-H	C_{10}-Methylene
IIa	257 ($W_{1/2}$ ~20 cps)	55	...	209.2, 219.9 (d) 226.2, 237.4 (d)
IIb	260 ($W_{1/2}$ ~15 cps)	47	200–240	200–240

B. 3α,5α-Cyclo Steroids

Compd		Cyclopropyl	C_{13}-Methyl	C_6-H	C_{17}-H	$COCH_3$	C_{10}-Methylene
Va[c]		30–50	68	208	237	...	210 (d),[d] 232 (d)[d]
Vc		20–50	53	274 (m)	274 (m)	123 (9H, s)	256 (2H, s)
IIIa		0–50	52	150.4, 152.7, 156.0 (t)	218	...	185.5, 197.0 (d) 207.6, 219.0 (d)
IV		0–50	54, 63[e]	141.0, 143.5, 146.6 (t)	...	...	...
IIIb	(1)	...[c]	42	230	278	121 (6H, s) 133 (3H, s)	238 (d),[d] 280 (d)[d]
	(2)	20–40	49	210	280	119, 122, 132	218 (d),[d] 275 (d)[d]
IIIc[c]		20–40	67	237	237	120	235 (d),[d] 208 (d)[d]

[a] Spectra were determined with a Varian A-60 spectrometer. Unless otherwise specified, deuteriochloroform was used as solvent. Chemical shifts are reported in cycles per second relative to tetramethylsilane as an internal reference. [b] In all cases of overlapping multiplets in spectra determined in deuteriochloroform solution assignments of the chemical shifts of the C_6 protons of the 3α,5α-cyclo steroids are based on those of model compounds reported in ref 6a. Chemical shifts of the 17α protons of the 17β acetates and 17β ols are consistent with the chemical shift of the 17α proton of dihydrotestosterone acetate reported by N. S. Bhacca, L. F. Johnson, and J. N. Shoolery ("N.M.R. Spectra Catalogue," Vol. I, Varian Associates, Palo Alto, Calif., 1962, Spectrum No. 353) and that of the 17α proton of testosterone reported by N. S. Bhacca and D. H. Williams ("Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, p 78). [c] Spectrum determined in pyridine-d_5 solution. [d] Approximate doublet centers. [e] C_{10}-CH_3 and C_{13}-CH_3.

hydrous benzene led to formation of the Δ^5-3β-*p*-toluenesulfonoxy-19-hydroxy steroids (IIa and IIb) in essentially quantitative yields.

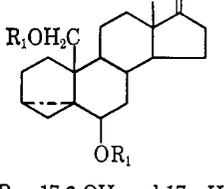
Ammonolysis of IIb with a large excess of ammonia led to the isolation of 6β-amino-17β,19-dihydroxy-3α,5α-cycloandrostane (IIIa) in 40% yield. The nmr spectrum (Table I) of this product showed the presence of cyclopropyl proton absorption, the absence of vinyl proton absorption, the AB quartet due to the absorption of the nonequivalent C_{19} protons, and the triplet absorption of the C_6 proton which is characteristic of 6β-substituted 3α,5α-cyclo steroids.[6]

The *cis*-1,3-diaxial relationship of the C_{10}-hydroxymethyl group and the 6β-amino group of IIIa was directly established by the occurrence of intramolecular hydrogen bonding between the 19-hydroxyl and the 6β-amino groups evidenced in infrared spectra determined in dilute carbon tetrachloride solution. The hydrogen-bonded absorption of IIIa occurred at 3225 cm^{-1}, while a model compound, 6β-amino-17-ethylenedioxy-3α,5α-cycloandrostane,[7] showed no absorption between 3100 and 4000 cm^{-1}. The lower frequency of the hydrogen-bonded hydroxyl absorption of the hydroxy amine (IIIa), compared with that of 6β,19-dihydroxy-3α,5α-cycloandrostan-17-one (Vb)[5b] ($\tilde{\nu}$ 3463 cm^{-1}), is consistent with comparisons of other related hydroxy amines and diols.[8]

As in the case of the 6β-hydroxy-3α,5α-cyclo steroids,[5b] the 19-hydroxy amine (IIIa) could be related to the C_{10}-methyl series by comparison of the chemical shifts and multiplet absorption patterns of the C_6 protons of IIIa and 6β-amino-17-ethylenedioxy-3α,5α-cycloandrostane (IV), in their nmr spectra (Table I), although the stronger hydrogen bonding in the hydroxy amine (IIIa) compared with the diol (Vb) results in a paramagnetic shift of about 9 cps of the C_6 proton of IIIa relative to that of the 10-methylamine (IV). These data provide an unambiguous proof of the configuration at C_6 of steroid 3α,5α-cyclo-6-amines.

The hydroxy amine (IIIa) was further characterized by its conversion to the diacetoxy acetamide (IIIb) which was readily hydrolyzed to the dihydroxy acetamide (IIIc). The nmr spectra of these products (Table I) were consistent with those of the 6β-acetamido-3α,5α-cyclo steroids previously reported.[6a,7]

Nitrous acid deamination of IIIa with excess sodium nitrite in 1:1 glacial acetic acid–water solution led to 46% deamination together with a 45% recovery of starting material. The deamination product was shown to be 6β,17β,19-trihydroxy-3α,5α-cycloandrostane (Va) by comparison with an authentic sample prepared by sodium borohydride reduction of the known[5a] 6β,19-dihydroxy-3α,5α-cycloandrostan-17-one (Vb). In the present work this latter compound was prepared by buffered hydrolysis of 3β-*p*-toluenesulfonoxy-19-hydroxyandrost-5-en-17-one (IIa).



Va, R_1 = H; R_2 = 17β-OH and 17α-H
b, R_1 = H; R_2 = O
c, R_1 = $COCH_3$; R_2 = 17β-$OCOCH_3$ and 17α-H

These results establish that in both ammonolysis and deamination reactions, as in kinetically controlled hydrolysis,[4] the stereochemistry of reaction at C_6 of steroid 3α,5α-cyclo-6-carbinyl cations is not significantly altered by the presence of a hydroxyl group at C_{19}.

(6) (a) J. Tadanier and W. Cole, *ibid.*, **27**, 4610 (1962); (b) F.-X. Jarreau, C. Monnert, Q. K.-H. Huu, and R. Goutarel, *Bull. Soc. Chim. France*, 2155 (1964).

(7) J. Tadanier and W. Cole, *J. Org. Chem.*, **27**, 4624 (1962).

(8) M. Tichy in "Advances in Organic Chemistry: Methods and Results," Vol. 5, Interscience Publishers, Inc., New York, N. Y., 1965, p 115.

Experimental Section

Melting points were determined with a Fisher-Johns block. Optical rotations were determined with a Hilger and Watts polarimeter. Infrared spectra were obtained with a Perkin-Elmer Model 421 grating spectrophotometer with deuteriochloroform solutions unless otherwise specified. Woelm alumina (activity III) was used for column chromatography. The petroleum ether used in this work was a fraction boiling at 66–70°.

In the present work, the infrared studies on hydrogen bonding were carried out with both the diol Vb and 6β-amino-17β,19-dihydroxy-3α,5α-cycloandrostane (IIIa) in carbon tetrachloride solution. In both cases the molar extinction coefficients of the hydrogen-bonded hydroxyl absorptions were independent of concentration when the measurements were carried out with 0.00125, 0.000625, and 0.000312 *M* solutions. The author is indebted to Mr. William Washburn for these determinations.

6β,19-Oxido-17β-hydroxy-3α,5α-cycloandrostane (Ib).—A solution of 1.0 g of 6β,19-oxido-3α,5α-cycloandrostan-17-one (Ia)[5a] in 70 ml of methanol was stirred in an ice bath and a freshly prepared solution of 1.82 g of sodium borohydride in 20 ml of water was added. Stirring was continued with the reaction vessel in an ice bath for 40 min. The product (Ib, 1.0 g, mp 182–183°) was isolated by ether extraction. The analytical sample, prepared by recrystallization from benzene–petroleum ether, melted at 182–184°: $[\alpha]^{24}D$ +68° (1% chloroform); $\tilde{\nu}_{max}$ 3613, 3053, 3026 cm^{-1}. *Anal.* Calcd for $C_{19}H_{28}O_2$: C, 79.13; H, 9.79. Found: C, 79.04; H, 10.01.

3β-*p*-Toluenesulfonoxy-17β,19-dihydroxyandrost-5-ene (IIb).—A solution prepared from 4.0 g of *p*-toluenesulfonic acid monohydrate and 200 ml of benzene was heated under reflux for 1 hr using a water separator and then allowed to cool to room temperature. To the resulting solution was added with stirring a solution of 2.01 g of 6β,19-oxido-17β-hydroxy-3α,5α-cycloandrostane (Ib) in 200 ml of benzene over a period of 10 min. After the addition was complete, stirring was continued for 15 min and the resulting solution was diluted to 500 ml with benzene and shaken with 600 ml of water. The benzene solution was washed with water, 5% sodium bicarbonate solution, and to neutrality with water, then combined and dried over anhydrous magnesium sulfate. Evaporation of the benzene left 3β-*p*-toluenesulfonoxy-17β,19-dihydroxyandrost-5-ene (IIb) which was crystallized by trituration with petroleum ether to yield 3.2 g: mp 125–126° dec; $\tilde{\nu}_{max}$ 3611, 1353, 1173, 1186 cm^{-1}. *Anal.* Calcd for $C_{26}H_{36}O_5S$: C, 67.80; H, 7.88; S, 6.96. Found: C, 67.58; H, 7.96; S, 6.74.

6β-Amino-17β,19-dihydroxy-3α,5α-cycloandrostane (IIIa).—3β-*p*-Toluenesulfonoxy-17β,19-dihydroxyandrost-5-ene (IIb, 3.2 g) was heated in an autoclave with 70 ml of liquid ammonia at 100° for 16 hr. The ammonia was evaporated and the residue was shaken with a mixture of ether and 2.5% sodium hydroxide solution. The aqueous phase was separated and extracted with ether. The ether solutions were washed with water, then combined, and concentrated to 200 ml. The resulting solution was extracted with 0.16 *M* hydrochloric acid solution. The aqueous phase was separated and extracted with ether.

The ether solutions were washed with water, 5% sodium bicarbonate solution, and then to neutrality with water, then combined, and dried over anhydrous magnesium sulfate. Evaporation of the ether left the neutral fraction (165 mg) as an orange oil.

The aqueous solution containing the amine hydrochloride was treated with carbon, briefly warmed on the steam bath, and then filtered through a Celite mat which was washed with hot 0.16 *M* hydrochloric acid, and the washings were added to the original filtrate. The resulting aqueous solution was cooled to room temperature and made basic by addition of 2.5% sodium hydroxide solution. The resulting suspension was extracted with ether. The ether solution was washed with water and then dried over anhydrous magnesium sulfate. Evaporation of the ether left 1.07 g of a white, crystalline solid. Recrystallization of this material from methanol–water solution gave 802 mg of 6β-amino-17β,19-dihydroxy-3α,5α-cycloandrostane (IIIa), mp 190–192°. The analytical sample, prepared by two additional recrystallizations from methanol–water solution, melted at 192–193°; $[\alpha]^{24}D$ +52° (1% chloroform); $\tilde{\nu}_{max}$ 3623, 3243, 3053, 3013 cm^{-1} (CCl_4). *Anal.* Calcd for $C_{19}H_{31}NO_2$: C, 74.72; H, 10.23; N, 4.59. Found: C, 74.61; H, 9.97; N, 4.65.

6β-Acetamido-17β,19-diacetoxy-3α,5α-cycloandrostane (IIIb).—To a solution of 206 mg of 6β-amino-17β,19-dihydroxy-3α,5α-cycloandrostane (IIIa) in 10 ml of pyridine was added 3.8 ml of acetic anhydride. The resulting solution was allowed to stand overnight at room temperature. The product was isolated by ether extraction to yield 280 mg of IIIb which melted at 164–169°. The analytical sample, prepared by recrystallization from acetone–petroleum ether, melted at 170–171°: $[\alpha]^{24}D$ +35° (1% chloroform); $\tilde{\nu}_{max}$ 3433, 1725, 1658, 1521 cm^{-1}. *Anal.* Calcd for $C_{25}H_{37}NO_5$: C, 69.56; H, 8.46; N, 3.25. Found: C, 69.59; H, 8.48; N, 3.36.

6β-Acetamido-17β,19-dihydroxy-3α,5α-cycloandrostane (IIIc).—A solution of 306 mg of 6β-acetamido-17β,19-diacetoxy-3α,5α-cycloandrostane (IIIb) in 15 ml of 5% methanolic potassium hydroxide was heated under reflux for 1 hr. The product (221 mg of IIIc, mp 262–263°) was isolated by ether extraction. The analytical sample, prepared by recrystallization from ethanol–water solution, melted at 263–264°: $[\alpha]^{24}D$ +2° (1% pyridine); $\tilde{\nu}_{max}$ 3621, 3347, 3063, 1649, 1543 cm^{-1}. *Anal.* Calcd for $C_{21}H_{33}NO_3$: C, 72.58; H, 9.57; N, 4.03. Found: C, 72.61; H, 9.62; N, 4.07.

3β-*p*-Toluenesulfonoxy-19-hydroxyandrost-5-en-17-one (IIa).—A solution of 2 g of *p*-toluenesulfonic acid monohydrate in 100 ml of benzene was heated under reflux for 45 min using a water separator. The resulting solution was cooled to room temperature and a solution of 1.02 g of 6β,19-oxido-3α,5α-cycloandrostan-17-one (Ia)[5a] in 100 ml of benzene was added dropwise with stirring over a period of 15 min. The product was isolated as described for the preparation of 3β-*p*-toluenesulfonoxy-17β,19-dihydroxyandrost-5-ene (IIb). The product, 3β-*p*-toluenesulfonoxy-19-hydroxyandrost-5-en-17-one (IIa, 1.55 g), melted at 135–138° dec; $\tilde{\nu}_{max}$ 3623, 1733, 1352, 1178 cm^{-1}. *Anal.* Calcd for $C_{26}H_{34}O_5S$: C, 68.10; H, 7.47; S, 6.99. Found: C, 68.38; H, 7.43; S, 6.88.

6β,19-Dihydroxy-3α,5α-cycloandrostan-17-one (Vb).—A solution prepared from 1.54 g of 3β-*p*-toluenesulfonoxy-19-hydroxyandrost-5-en-17-one (IIa), 154 ml of acetone, 70 ml of water, and 1.54 g of potassium acetate was heated under reflux for 18 hr. The solution was then cooled and diluted with 150 ml of water and the major portion of the acetone was removed under aspirator pressure. The product was isolated by ether extraction to yield 1.06 g of a pale yellow glass. This material was heated under reflux for 1 hr in 100 ml of 5% methanolic potassium hydroxide solution. The resulting solution was cooled and diluted with 100 ml of water, the major portion of the methanol was evaporated under reduced pressure, and the product was isolated by ether extraction to yield 997 mg of a pale yellow glass.

This product was chromatographed on 200 g of alumina. Elution with 1:1 ether–benzene solution gave 790 mg of 6β,19-dihydroxy-3α,5α-cycloandrostan-17-one (Vb), mp 169–171° (lit. 171–173°,[5b] 175–175.5°[5a]). The nmr spectrum of this material was identical with that of material previously reported.[5b]

6β,17β,19-Trihydroxy-3α,5α-cycloandrostane (Va).—A solution of 757 mg of 6β,19-dihydroxy-3α,5α-cycloandrostan-17-one (Vb) in 80 ml of methanol was cooled in an ice bath and a freshly prepared solution of 2.62 g of sodium borohydride in 30 ml of water was added with stirring. Stirring was then continued for 45 min with the reaction vessel in an ice bath. The product was isolated by ether extraction as a white glass which separated as a gel on attempted recrystallization from acetone–petroleum ether. The supernatant was decanted and the gel was dried to a white, amorphous powder. This product [485 mg of 6β,17β,19-trihydroxy-3α,5α-cycloandrostane (Va)] liquified between 121 and 128°, $[\alpha]^{25}D$ +44° (1% pyridine) and gave a single spot on tlc (1:3 benzene–ethyl acetate on silica gel G). *Anal.* Calcd for $C_{19}H_{30}O_3$: C, 74.48; H, 9.87. Found: C, 74.72; H, 9.80.

The triacetate (Vc) was prepared by treatment of 200 mg of Va with 3.8 ml of acetic anhydride in 10 ml of pyridine at room temperature for 20 hr and was isolated by ether extraction to yield an oil, $[\alpha]^{26}D$ +37° (1% chloroform), which gave a single spot on tlc (7:3 benzene–ethyl acetate on silica gel G); $\tilde{\nu}_{max}$ 3065, 1718, 1250 cm^{-1}. *Anal.* Calcd for $C_{25}H_{36}O_6$: C, 69.41; H, 8.39. Found: C, 69.19; H, 8.50.

Deamination of 6β-Amino-17β,19-dihydroxy-3α,5α-cycloandrostane (IIIa).—A solution of 308 mg of 6β-amino-17β,19-dihydroxy-3α,5α-cycloandrostane (IIIa) in 15 ml of 1:1 acetic acid–water solution was cooled in an ice bath to 0–5° and a freshly prepared solution of 1.23 g of sodium nitrite in 15 ml of 1:1 acetic acid–water solution (precooled to 0–5°) was added. The resulting solution was allowed to stand at room temperature for 1 hr. The resulting, cloudy suspension was shaken with a mixture of water and ether, and the aqueous phase was separated.

The ether solution was washed with water, the first aqueous wash was combined with the original aqueous extract, and the resulting aqueous solution containing unreacted amine was set aside.

The ether solutions were then washed with 5% sodium bicarbonate solution and to neutrality with water, then combined and dried over anhydrous magnesium sulfate. Evaporation of the ether left 167 mg of an oil. This product was heated under reflux for 1 hr with 5% methanolic potassium hydroxide solution. The product was isolated by ether extraction as a white glass (141 mg, 46%). This material was identified as 6β,17β,19-trihydroxy-3α,5α-cycloandrostane (Va) by comparison of infared (KBr pellet) and nmr spectra (pyridine-d_5 solution) and its behavior on thin layer chromatography with that of authentic material prepared as described above. Tlc allowed the estimate that less than 10% of by-products was present in the sample. In addition, the deamination product was converted to the triacetate (Vc, oil) with acetic anhydride in pyridine. The infrared and nmr spectra and behavior of this material on thin layer chromatography were essentially identical with those of the triacetate (Vc) prepared as described above.

The aqueous solution containing the unreacted amine was made basic with 5% aqueous sodium hydroxide solution and the resulting solution was extracted with ether. The ether solution was washed with water and dried over anhydrous magnesium sulfate. Evaporation of the ether left 139 mg (45%) of 6β-amino-17β,19-dihydroxy-3α,5α-cycloandrostane (IIIa) which was identified by comparison of its infrared and nmr spectra with those of the starting material. The behavior of the recovered amine on thin layer chromatography on both silica gel (75:25 benzene–methanol, trace ammonium hydroxide) and alumina (85:15 benzene–methanol, trace ammonium hydroxide) was identical with that of the starting amine IVa.

Registry No.—Ib, 10076-03-6; IIa, 10076-07-0; IIb, 10076-04-7; IIIa, 10076-02-5; IIIb, 10076-05-8; IIIc, 10076-06-9; IV, 2686-03-5; Va, 10076-08-1; Vc, 10076-09-2.

Acknowledgment.—The author wishes to thank Mr. W. Washburn and associates for the infrared spectra, Mrs. Ruth Stanaszek for the nmr spectra, and Mr. O. Kolsto and co-workers for elemental analyses. Thin layer chromatographies were carried out by Mrs. Evelyn Baker and Miss Judy Wolf. Thanks are due Mr. D. A. Dunnigan for carrying out the ammonolysis reaction.

Structure of Homodimers of Thymine and Dimethylthymine. A Nuclear Magnetic Resonance Study

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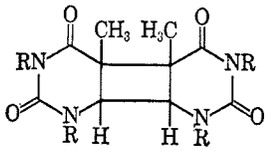
Received October 13, 1966

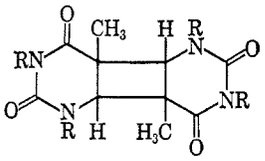
The possible correlation between the biological consequences of ultraviolet irradiation and the appearance of thymine homodimer[1] (T=T) in irradiated DNA has attracted widespread interest.[2-4] To understand this photobiological phenomenon in chemical terms, a determination of the exact stereoconfiguration of T=T is necessary.[5] Early studies of T=T isolated from thymine irradiated with ultraviolet light in frozen, aqueous solutions or as solid films suggested the *cis–syn* configuration.[6,7] This assignment was based on the photochemical behavior of thymine which exists as monohydrate crystals (Figure 1) as was determined by X-ray crystallography.[8] Recently, Blackburn and Davies[9] assigned the same configuration based on the rearranged products of T=T.

Anet[10] reported the use of the naturally abundant C^{13}–H satellite proton spectrum for determining the coupling constant $J_{H_1H_2}$ between the two cyclobutane protons. While this method cannot yield information about *cis* or *trans* configuration, it can provide the most direct evidence for *syn* or *anti* configuration. To determine the stereoconfiguration of T=T, Anet used only the high-melting 1,3-dimethylthymine homodimer (I). [This compound is formed in equal proportion with the low-melting DMT=DMT (II) obtained from the ultraviolet irradiation of 1,3-dimethylthymine (DMT) in frozen solution.[11,12]] The use of I as a reference for assigning the structure of T=T was based on the fact that it is the sole product resulting from the methylation of T=T.[12] However, this approach is subject to the criticism by Smith[2] that I might not be the isomer corresponding to T=T, an isomer that could conceivably be lost during the low-yield methylation process. Therefore, it seems to be necessary to determine directly the configuration of T=T itself.

In the present work, the 100-Mcps nmr spectra of I, II, and T=T were obtained on 3% (w/w) solution in CF_3COOD. The chemical shifts and assignments are presented in Figure 2, and agree with those given by



syn
I, R = CH_3
T=T, R = H



anti
II

Wulff and Fraenkel.[12] To our knowledge, this paper is the first report of spectra for all the dimers using a single solvent and a single reference sample. It is interesting to note that our data have revealed the possibility of obtaining information about the configuration of these dimers simply by comparing the chemical shifts of their cyclobutane protons. The chemical shift of the protons of I is within 0.09 ppm that of T=T, but differs by 0.59 ppm from that of II while the C–CH_3 resonances of all three compounds are within 0.08 ppm. This parallelism suggests that I and T=T should possess one arrangement and II should possess the other.

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