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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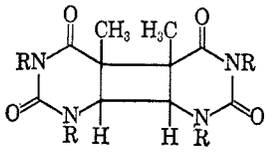
Received October 13, 1966

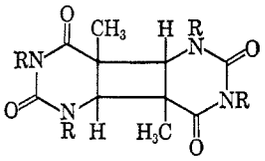
The possible correlation between the biological consequences of ultraviolet irradiation and the appearance of thymine homodimer[1] (T=T) in irradiated DNA has attracted widespread interest.[2-4] To understand this photobiological phenomenon in chemical terms, a determination of the exact stereoconfiguration 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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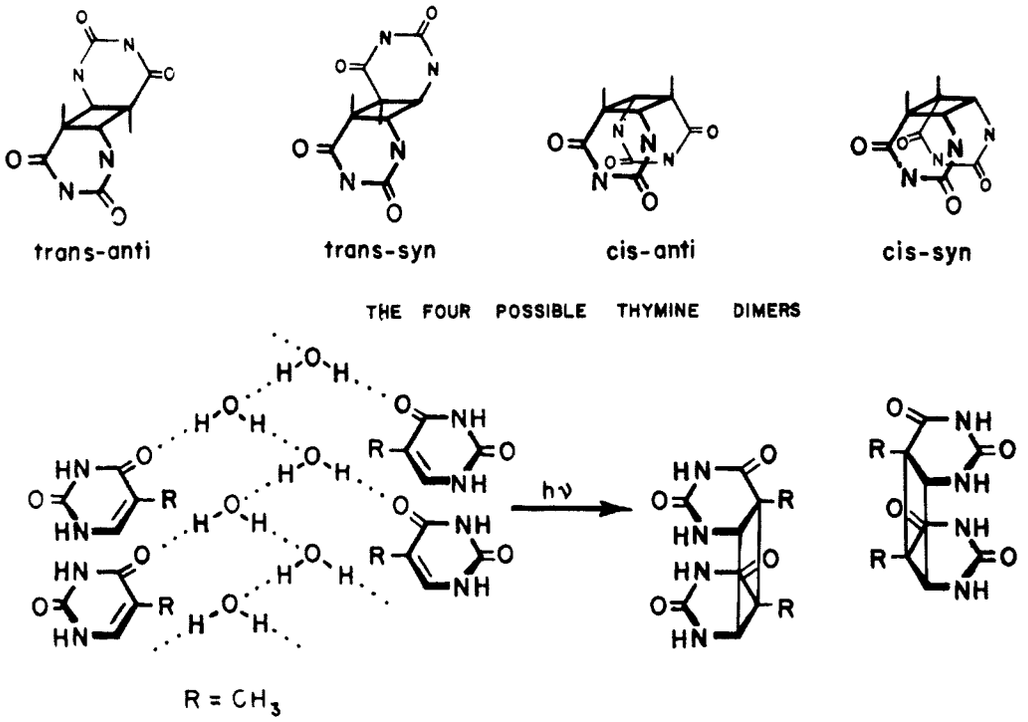

Figure 1.

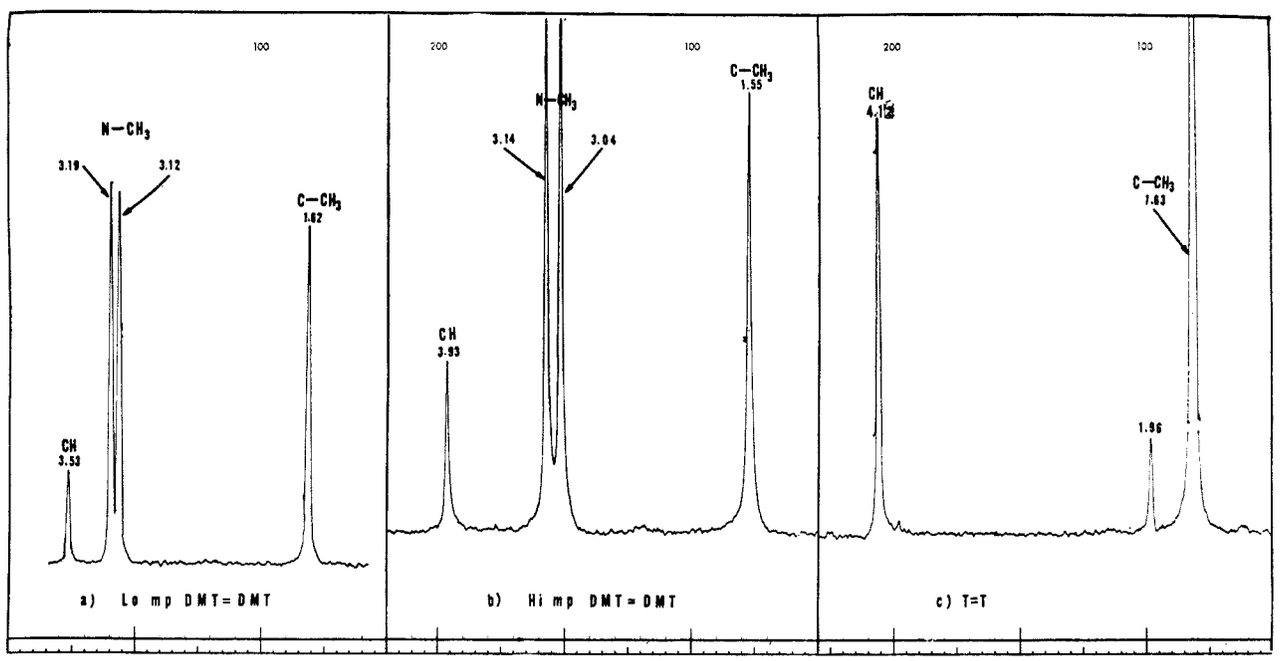

Figure 2.—Nmr spectra (100 Mcps) of (a) low-melting point DMT=DMT; (b) high-melting DMT=DMT; and (c) T=T. These spectra were obtained using 3% (w/w) solutions of the dimers in CF_3COOD. Chemical shifts are given relative to external tetramethylsilane.

From the naturally abundant C^{13}–H satellite spectra of these three dimers (Figure 3) the coupling constants between the two cyclobutane CH can be measured directly.[13] Low-melting DMT=DMT shows a single C^{13}–H satellite peak. Since the coupling constant between the 1,3 protons is expected to be approximately 0,[14] the arrangement of II should be *anti* or head to tail. On the other hand, I gave a doublet C^{13}–H satellite (J = 4.8 ± 0.5 cps) which is consistent with a *syn* or 1,2 arrangement of the two cyclobutane ring protons.[10,15] Since thymine homodimer from frozen solutions and solid films also gave doublet C^{13}–H satellite

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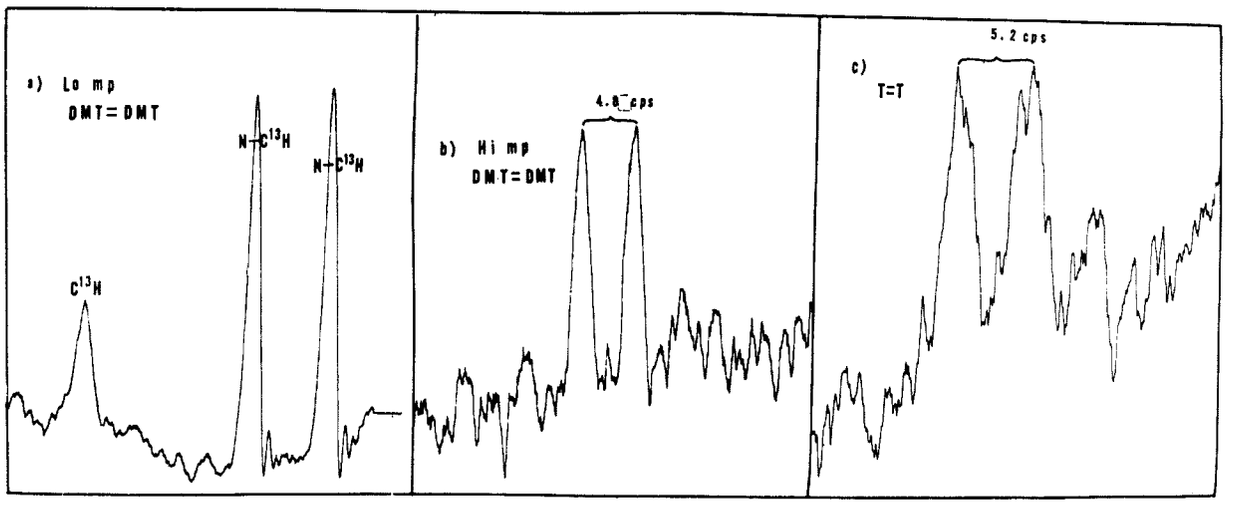

Figure 3.—Low-field C^{13}–H satellite spectra: (a) low-melting DMT=DMT, 10% (w/w) in $CDCl_3$, 300 runs; (b) high-melting DMT=DMT, 10% (w/w) in $CDCl_3$, 50 runs; (c) T=T, 3% (w/w) in CF_3COOD, 64 runs.

peaks (J = 5.2 ± 0.5 cps), T=T must also have the *syn* or head-to-head arrangement. The several coupling constants measured for the three dimers are given in Table I. The C^{13}–H coupling constants are accurate to ±2 cps. The coupling constants for I agree, within the range of experimental error, with those reported by Anet.[10]

TABLE I
COUPLING CONSTANTS OF THE THREE DIMERS

Dimer		$J_{C^{13}H}$, cps	$J_{NC^{13}H}$, cps	J_{HH} (cyclobutane), cps
Low-melting	DMT=DMT	155	148, 150	0
High-melting	DMT=DMT	151	140, 142	4.8 ± 0.5
T=T		158	...	5.2 ± 0.5

Experimental Section

T=T and Mixture of DMT=DMT Isomers.—Dimers from frozen, aqueous solutions and T=T from solid films were prepared as previously described.[11]

Separation of DMT=DMT Isomers.—The residue from the irradiated frozen solutions of 3 l. of 0.1 *M* DMT was dissolved in chloroform and mixed with 1 g of acid-washed alumina. After removal of the excess chloroform, the mixture was placed on the top of a 19 cm × 1.8 cm^2 column of acid-washed alumina and eluted with ether (1.4 l.), 0.2% ethanol–ether (1.6 l.), and chloroform. About 40% of the starting material was recovered from the ether fraction. The 0.2% ethanol–ether fraction yielded a product with mp 225–226° (low-melting DMT=DMT) after crystallization from chloroform–petroleum ether (bp 30–60°). From the chloroform fraction, an isomer with mp 258–259° (high-melting DMT=DMT) was obtained. The two isomers were present in equal amounts and the total yield was 50–60%.

Nmr Spectra.—These spectra were obtained on the Varian HA-100 spectrometer operating in the field-sweep mode. Chemical shifts were measured directly from the precalibrated charts. Naturally abundant C^{13}–H satellites were observed by time averaging a 50-cps region beginning 100 cps to low field of the cyclobutane CH peaks using the Varian C-1024 time-averaging computer. Fifty runs were sufficient to give acceptable spectra for the 3–10% concentrations employed.

Registry No.—Thymine homodimer, 7721-75-7; I (R = CH_3), 7721-76-8; II (R = CH_3), 7721-77-9.

Acknowledgment.—The authors thank Mr. Patrick Pellow for his able assistance. This work was supported in part by Contract AT(30-1)-2798 from the U. S. Atomic Energy Commission and also by a Career Development Award (Division of General Medical Science) and a Research Grant (No. HE 06079) to Dr. W. S. Caughey from the U. S. Public Health Service.

The Reaction of Trifluoromethyl Ketones with Resonance-Stabilized Alkylidene Phosphoranes[1]

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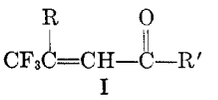
Received December 7, 1966

We wish to report a convenient and general synthesis of trifluoromethyl-containing α,β-unsaturated carbonyl compounds of type I. Certain compounds of this type



$$CF_3C(R)=CH-C(=O)-R'$$

I

where R′ is OH or OC_2H_5 have been reported.[2–6] The Knovenagel condensation with trifluoromethyl ketones leads to β-hydroxy acids instead of α,β-unsaturated acids. Some of these β-trifluoromethyl-β-hydroxy acids and esters have proven very resistant to dehydration and we therefore were forced to find another general route to such compounds.

It was found that trifluoromethyl ketones readily react with resonance-stabilized alkylidene phosphoranes. To the best of our knowledge only one Wittig reaction of this type has been reported, namely the reaction of hexafluoroacetone with acetylmethylenetri-

(1) We gratefully acknowledge support for these studies by the U. S. Public Health Service (GM-05248) and the National Science Foundation (GP 3888).

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