Anal. Calcd for $C_{19}H_{18}N_4O_4 \cdot H_2O$: C, 59.37; H, 5.24; N, 14.58. Found: C, 59.29; H, 5.37; N, 13.42.

Direct comparative irradiations of 1, 4, 6, and 8 and of 1-propylthymine were carried out under nitrogen in separate Pyrex test tubes on a circularly rotating reaction table which ensured constancy of the absorbed light intensity. The monomer concentrations were identical with those used in the photosensitized reactions (1 m*M* for **1**, **4**, **6**, and **8** and 2 m*M* for 1-propylthymine). Ultraviolet absorption characteristic of the undimerized starting materials diminished in a well-mannered first-order fashion. Using our apparatus, the irradiation of **4**, **6**, and **8** could not be practically carried to completion. Relative first-order half-reaction times reported in the Discussion, *i.e.*, 26, 1, and 7.5 for compounds **4**, **1**, and **6**, respectively, are averaged values from three or more independent runs on these compounds measured simultaneously.

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Crystal and Molecular Structure of 1,1′-Trimethylenebisthymine (Thy-C$_3$-Thy). A Study of the Environment of a Solid State Photochemical Reaction[1]

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Abstract: The crystal structure of 1,1′-trimethylenebisthymine (**1**), Thy-C$_3$-Thy, has been determined to provide information on the base–base interaction and to establish the lattice environment of the reactant in a solid state photochemical process. The crystals of **1** are monoclinic with a = 7.144 (1), b = 16.734 (3), c = 12.067 (2) Å, and β = 112° 39′ (1′); the space group is $C2/c$. The structure was solved by the symbolic addition method and has been refined to an R factor of 0.034 on 895 nonzero reflections measured on a diffractometer. Disorder in the position of the atoms of the trimethylene bridge permits the molecule to have C_2 crystallographic symmetry and substantial intramolecular overlap of the two thymine rings. The dimensions, conformation, and crystal packing of the thymine moieties are described and compared with those found in other thymine derivatives. The thymine rings in the crystal of **1** are arranged such that both intramolecular and intermolecular photoreaction could occur, although in each case trans–syn geometry for the product would be anticipated. Chemical studies indicate a polymeric product which would arise from intermolecular reaction. A comparison of the intra- and intermolecular ring–ring interactions is given in the light of this finding.

A series of dinucleotide analogs, base-C$_3$-base or base(1-(CH$_2$)$_3$-1) base, were synthesized by Leonard and coworkers to investigate various interactions between nucleic acid bases under the constraints imposed by the trimethylene bridge.[3] One of these analogs, Thy-C$_3$-Thy (**1**), undergoes photoreaction in dilute aqueous solution to an intramolecular dimer (**2**) with cis–syn geometry.[4] During the X-ray study of the structure of **2**, it was observed that, in the crystal, **2** reverted to **1** to the extent of about 10%. An X-ray study of **1** was undertaken to determine the conformation of **1** in the crystal in order to assess the forces influencing conformation in this analog of thymidylyl(3′–5′)thymidine (TpT). The structural results so obtained served to initiate an investigation of the solid state photoreaction as topochemical considerations would predict a product having trans–syn (as in **3**) rather than cis–syn geometry. The chemical aspects of this study are reported in the preceding paper.[5]

Experimental Section

The crystals of **1** (mp 330–332°[3]) obtained from aqueous solution are colorless, transparent, almost hexagonal-shaped plates with rounded edges. The developed face of the plate is (100). Crystal data: $C_{13}H_{16}N_4O_4$, M = 292.3; monoclinic, a = 7.144 (1), b = 16.734 (3), c = 12.067 (2) Å; β = 112° 39′ (1′); V = 1331.2 × 10^{-24} cm^3, ρ_{measd} (flotation in a hexane–carbon tetrachloride mixture) = 1.45 g cm^{-3}; Z = 4; ρ_{calcd} = 1.46 g cm^{-3}; $F(000)$ = 616, μ (Cu Kα) = 9.4 cm^{-1}. With systematic absences for hkl when $h + k = 2n + 1$ and for $h0l$ when $l = 2n + 1$, the space group is either $C2/c$ or Cc.

A platelet crystal, 0.04 × 0.20 × 0.45 mm, was mounted about the elongated c axis on a Picker FACS-1 diffractometer. The cell dimensions were determined by a least-squares fit to the angular settings for ten reflections. Approximately monochromatic Cu Kα (λ 1.5418 Å) radiation was obtained by use of a nickel filter and pulse height analysis, and the diffracted intensities were measured on a scintillation counter with attenuators being inserted when necessary. The octants of data, $h\bar{k}\bar{l}$ and $\bar{h}\bar{k}\bar{l}$, to 2θ = 130° were measured at ambient room temperature by means of a moving crystal–moving counter technique, with a 2θ scan rate of 1°/min and 10-sec background counts at each end of the scan. The monitoring of a standard reflection after every 30 measurements indicated that no crystal decomposition occurred during data collection. Of 1113 possible unique reflections, 895 were considered to be significantly above background, *i.e.*, 200 net counts or 10%

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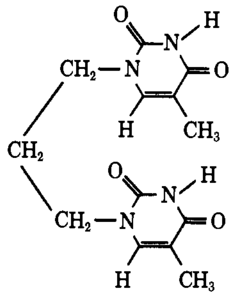
Table I. Final Positional Parameters with Standard Deviations in Parentheses

	x	y	z
N(1)	0.2294 (3)	0.03137 (10)	0.82367 (16)
C(2)	0.2585 (4)	0.06380 (13)	0.93368 (19)
N(3)	0.2725 (3)	0.14590 (11)	0.93890 (16)
C(4)	0.2549 (3)	0.19734 (13)	0.84576 (19)
C(5)	0.2374 (3)	0.15887 (13)	0.73489 (19)
C(6)	0.2263 (4)	0.07878 (13)	0.72976 (19)
C(7)	0.1963 (4)	−0.05596 (13)	0.80596 (25)
C(8)	−0.0080 (9)	−0.07971 (27)	0.80227 (45)[a]
O(9)	0.2708 (3)	0.02397 (10)	1.02065 (15)
O(10)	0.2578 (3)	0.27017 (9)	0.86075 (14)
C(11)	0.2274 (5)	0.20895 (16)	0.62968 (22)
H(3)	0.270 (4)	0.1682 (15)	1.0063 (24)
H(6)	0.216 (3)	0.0483 (13)	0.6579 (21)
H(11A)	0.213 (5)	0.1754 (18)	0.5580 (28)
H(11B)	0.115 (5)	0.2467 (19)	0.6073 (26)
H(11C)	0.348 (4)	0.2367 (17)	0.6440 (24)
H(7A)	0.233 (8)	−0.068 (3)	0.720 (5)[a,b]
H(7B)	0.301 (8)	−0.085 (3)	0.874 (5)[a,b]
H(7C)	0.184 (10)	−0.074 (3)	0.889 (5)[a]
H(7D)	0.319 (7)	−0.079 (3)	0.802 (5)[a]
H(8A)	−0.030 (8)	−0.058 (3)	0.882 (5)[a]
H(8B)	−0.015 (9)	−0.135 (3)	0.808 (5)[a]

[a] Indicates that atom was included in structure factor calculations at half-weight. [b] H(7C) and H(7D) are the alternative sites from H(7A) and H(7B) due to the disorder of the central carbon atom of the methylene chain.



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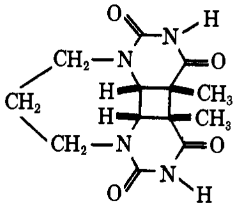

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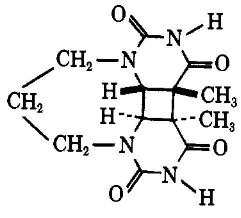

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Table II. Final Thermal Parameters[a,b] with Standard Deviations in Parentheses

	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
N(1)	0.0197 (5)	0.00173 (6)	0.0048 (2)	−0.0003 (3)	0.0070 (5)	−0.0002 (2)
C(2)	0.0185 (6)	0.00229 (8)	0.0045 (2)	−0.0007 (4)	0.0062 (5)	0.0000 (2)
N(3)	0.0221 (6)	0.00220 (7)	0.0034 (2)	−0.0019 (3)	0.0074 (5)	−0.0008 (2)
C(4)	0.0159 (6)	0.00227 (8)	0.0044 (2)	−0.0024 (3)	0.0065 (5)	−0.0006 (2)
C(5)	0.0161 (6)	0.00218 (8)	0.0038 (2)	−0.0017 (3)	0.0068 (5)	−0.0004 (2)
C(6)	0.0173 (6)	0.00238 (8)	0.0043 (2)	−0.0009 (4)	0.0079 (5)	−0.0011 (2)
C(7)	0.0238 (8)	0.00159 (8)	0.0076 (3)	0.0019 (4)	0.0082 (7)	0.0000 (2)
C(8)	0.0277 (15)	0.00119 (15)	0.0070 (4)	−0.0002 (8)	0.0107 (14)	0.0009 (4)
O(9)	0.0363 (6)	0.00290 (7)	0.0051 (2)	−0.0017 (3)	0.0116 (5)	0.0020 (2)
O(10)	0.0319 (5)	0.00183 (6)	0.0058 (2)	−0.0033 (3)	0.0130 (5)	−0.0013 (1)
C(11)	0.0244 (8)	0.00306 (10)	0.0048 (2)	−0.0035 (5)	0.0102 (7)	0.0005 (2)

	B_θ, Å^2		B_θ, Å^2		B_θ, Å
H(3)	3.7 (6)	H(11C)	4.8 (7)	H(7D)	1.9 (9)
H(6)	2.9 (5)	H(7A)	3.0 (1.1)	H(8A)	4.7 (1.3)
H(11A)	6.1 (8)	H(7B)	2.6 (1.0)	H(8B)	4.9 (1.3)
H(11B)	5.8 (8)	H(7C)	4.9 (1.3)		

[a] Anisotropic thermal parameters are expressed as $\exp[-(b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl)]$. [b] Isotropic parameters expressed as $\exp[-(B_\theta \sin^2 \theta/\lambda^2)]$.

above background, whichever is greater. Lorentz and polarization corrections were applied to the data, but no correction for absorption was made. A Friedel transformation was applied to the data before further use.

$C2/c$ was considered the more probable space group although such a choice would require disorder in the position of the central methylene group with respect to the twofold axis. The structure was solved, although not without difficulty, by the symbolic addition method[6] using the FAME–MAGIC–LINK–SYMPL programs.[7] It proved difficult to find a starting set of reflections which would provide sufficient interactions, or differentiation among the number of inconsistencies for different assignments of the starting symbols. Finally, using just five reflections in the starting set, a combination of signs which gave 23% inconsistencies appeared to be significantly better than the other sets. An E map based on 296 reflections revealed the positions of the nine atoms of the thymine residue plus the connecting carbon atom in the methylene bridge in a plane approximately perpendicular to the a axis at $x = {}^1/_4$. The central carbon atom of the trimethylene chain, C(8), was located near the special position (0, y, ${}^3/_4$) on a subsequent Fourier map. However, attempts to refine this model did not reduce the R factor below 0.43. A closer inspection of the Fourier map revealed, in addition to the included atoms, an image of the structure displaced by about 1.5 Å along the b axis. Upon careful examination, a similar image of the structure was observed in the original E map. The alternative position for the molecule did not provide a basis for successful refinement; the R factor could not be reduced below 0.44 and a Fourier map based on this position showed, in addition to the included atoms, an image of the molecule in the original position. This appears to be a case of a pseudo-homometric structure, described recently by Bürgi and Dunitz.[8] In such instances, the correct structure is an average of two "half-weight" variants displaced from each other by a prominent vector in the structure. Thereafter the structure refined smoothly. It became clear that C(8) was disordered in two positions slightly displaced from the twofold axis. Full-matrix least-squares refinement varying positional and isotropic temperature factors for the nonhydrogen atoms gave an R factor of 0.137 and R_2, $[\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$, of 0.142. All reflections were given unit weights and the quantity minimized was $\Sigma w(|F_o| - |F_c|)^2$.

The positions of five of the hydrogen atoms in the molecule were readily obtained from a difference map, but those of the hydrogen atoms attached to carbon atoms of the trimethylene chain could not

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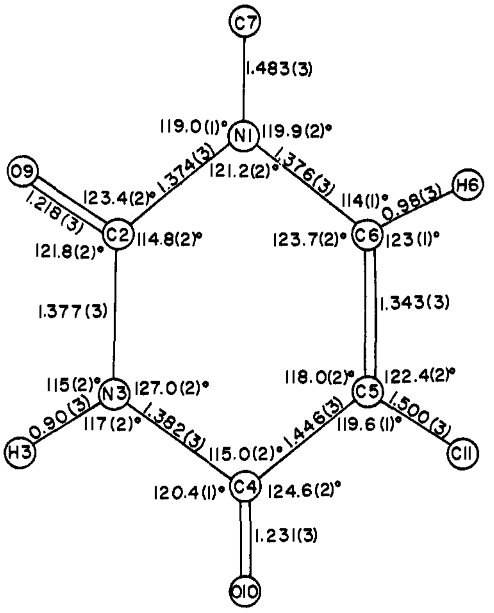

Figure 1. Bond lengths and angles in the thymine moiety. Lengths not given in figure are C(7)–C(8), 1.496 (7); C(7)–C(8′), 1.523 (7); C(11)–H(11A), 1.00 (3); C(11)–H(11B), 0.97 (4); C(11)–H(11C), 0.93 (3); C(7)–H(7A), 1.18 (5); C(7)–H(7B), 1.00 (6); C(7)–H(7C), 1.09 (6); C(7)–H(7D), 0.98 (5); C(8)–H(8A), 1.09 (6); and C(8)–H(8B), 0.94 (5) Å. Angles are N(1)–C(7)–C(8), 111.5 (3); N(1)–C(7)–H(7A), 103 (3); N(1)–C(7)–H(7B), 110 (3); N(1)–C(7)–H(7C), 102 (3); N(1)–C(7)–H(7D), 108 (3); C(8)–C(7)–H(7A), 118 (3); C(8)–C(7)–H(7B), 108 (3); C(8′)–C(7)–H(7C), 111 (3); C(8′)–C(7)–H(7D), 112 (3); H(7A)–C(7)–H(7B), 107 (4); H(7C)–C(7)–H(7D), 109 (4); C(7)–C(8)–C(7′), 119.0 (2); C(7)–C(8)–H(8A), 111 (3); C(7)–C(8)–H(8B), 110 (4); C(7′)–C(8)–H(8A), 107 (3); C(7′)–C(8)–H(8B), 106 (4); H (8A)–C(8)–H(8B), 104 (5); C(5)–C(11)–H(11A), 112 (2); C(5)–C(11)–H(11B), 111 (2); C(5)–C(11)–H(11C), 112 (2); H(11A)–C(11)–H(11B), 109 (3); H(11A)–C(11)–H(11C), 103 (3); and H(11B)–C(11)–H(11C), 109 (3)°.

be found at this stage. These atoms will be disordered as a consequence of the disordering of the central carbon atom. Introduction of anisotropic temperature factors for the non-hydrogen atoms and inclusion of the five hydrogen atoms with isotropic temperature factors in a least-squares refinement gave R of 0.082 and R_2 of 0.105. A further difference map at this stage provided the sites for the disordered hydrogen atoms, and their inclusion in the refinement gave an R factor of 0.034 and R_2 of 0.037. Prior to this last series of refinements, the reflection 200 was removed from the data used for refinement as it was judged to suffer from errors due to extinction. The final positional and thermal parameters are listed in Tables I and II, while the final values of hkl, $|F_o|$, and F_c are published in the microfilm edition of the journal.[9,10] The atomic scattering curves for carbon, nitrogen, and oxygen were taken from the compilation in "International Tables for X-ray Crystallography,"[11] while that for hydrogen was calculated by Stewart, *et al.*[12]

Results and Discussion

Bond Lengths and Angles in 1 and Other Thymine Derivatives. The bond lengths and angles found in this study are given in Figure 1 and a stereoscopic view of the molecular structure is shown in Figure 2. Several X-ray structure analyses on thymine derivatives have been reported; these include 1-methylthymine,[13] the 1:1 complex of 1-methylthymine and 9-methyladenine,[14] thymine monohydrate,[15] anhydrous thymine,[16] thymidine,[17] and the 1:1 complex of thymine and *p*-benzoquinone.[18] The relatively low accuracy (σ of bond length 0.015–0.019 Å) of the analyses of anhydrous thymine and of the *p*-benzoquinone–thymine complex make comparison involving these structures of limited value. In Table III some of the bond lengths and angles in **1** are compared with those found in 1-methylthymine, in the 1-methylthymine–9-methyladenine complex, in thymidine, and in thymine mnohydrate. As has been pointed out by both Gerdil[15] and Hoogsteen[13] the general pattern of bond lengths in thymine derivatives can be explained in terms of valence bond theory. Among the four compounds having a carbon atom substituent on N(1), the mean lengths of the four C–N bonds in the ring are 1.378–1.379 Å and the greatest diversity in bond length occurs for the C(4)–C(5) bond with a length of 1.422 (5) Å in the case of the 1-methylthymine–9-methyladenine complex and a length of 1.453 (6) Å in the case of thymidine. A comparison of lengths in thymine (from the monohydrate structure) with the N(1)-substituted thymine derivatives reveals significant differences ($>3\sigma$) in the lengths of the N(1)–C(2), C(2)–N(3), N(3)–C(4), and C(2)–O(9) bonds. In the case of N(1)–C(2) and C(2)–O(9) the differences are 5σ. Some of these changes have been attributed by Hoogsteen[13] to the difference in electronegativity between the carbon and hydrogen substituents on N(1). The differences in the C(2)–O(9) bond lengths may also be partially dependent on the nature of the hydrogen bonding involving O(9). In **1**, 1-methylthymine, and thymidine, this atom is not involved in hydrogen bonding, unless one admits C—H···O hydrogen bonding (see below), whereas in the case of thymine monohydrate, where both carbonyl bonds are of equal length, each is involved as a hydrogen bond acceptor. The argument that participation in hydrogen bonding causes elongation of the C=O bond fails to explain why, in the 1-methylthymine–9-methyladenine complex, the C(2)=O(9) bond is as short as 1.207 (5) Å when there is an N—H···O hydrogen bond involving O(9). It is possible, however, that less weight should be given to the results from this complex because in that crystal the molecules are constrained by symmetry to lie on mirror planes. Thus, there may either be minor disorder in the crystal, or the packing energy gained by the higher symmetry environment may have caused distortions from the minimum energy configuration associated with an isolated molecule. A recent survey by Voet and Rich[19] gives the mean lengths of the C(2)–O(9) and C(4)–O(10) bonds in a number of thymine and uracil derivatives as 1.219 and 1.233 Å. However,

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(9) The final list of hkl, $|F_o|$, and F_c will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JACS-73-2324. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

(10) A retrospective examination of the five reflections used to generate the signs of the 296 reflections for the E map revealed that two of them (0,12,5 and 1,11,5) were given incorrect signs in the initial assignment. It is also of interest that the other three starting reflections had even values for l.

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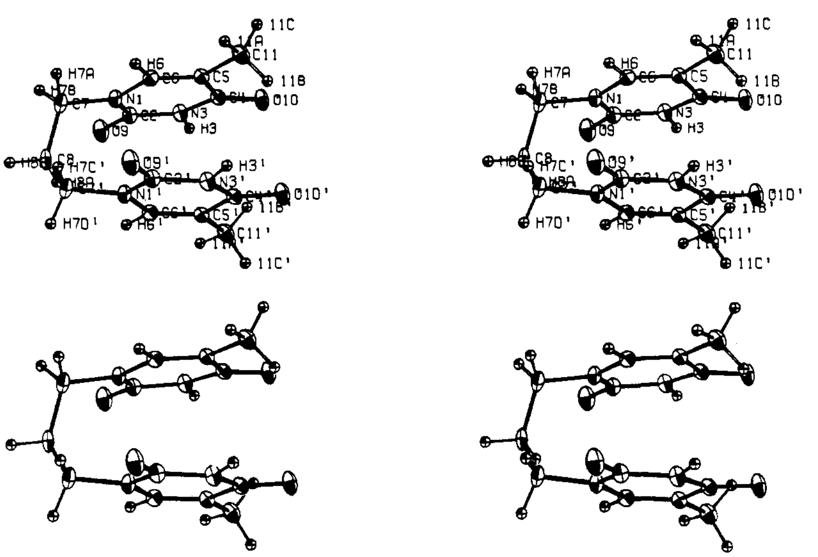


Figure 2. Stereoscopic picture of two molecules of **1** stacked along the *a* axis. The probability level of the thermal ellipsoids is 25%.

Table III. Comparisons of Bond Lengths (Å) and Angles (deg) in Some Thymine Derivatives^{a}

	1-Substituted thymines						
	1	1-Methylthymine^{b}	1-Methylthymine–9-methyladenine complex^{c}	Thymidine^{d}	Mean value Max dev^{e}	Thymine monohydrate^{f}	Diff^{g}
N(1)–C(2)	1.374 (3)	1.379 (4)	1.376 (5)	1.385 (6)	1.379 (11)	1.355 (5)	0.024
C(2)–N(3)	1.377 (4)	1.379 (4)	1.378 (5)	1.381 (7)	1.379 (4)	1.361 (4)	0.018
N(3)–C(4)	1.382 (3)	1.375 (4)	1.377 (5)	1.378 (7)	1.378 (7)	1.391 (3)	0.013
C(4)–C(5)	1.446 (3)	1.432 (4)	1.422 (5)	1.453 (6)	1.438 (31)	1.447 (5)	0.009
C(5)–C(6)	1.343 (3)	1.346 (4)	1.333 (5)	1.343 (7)	1.341 (13)	1.349 (5)	0.008
N(1)–C(6)	1.376 (3)	1.383 (4)	1.382 (5)	1.374 (6)	1.379 (9)	1.382 (4)	0.003
C(2)–O(9)	1.218 (3)^{h}	1.214 (3)^{h}	1.207 (5)^{i}	1.206 (7)^{j}	1.211 (12)	1.234 (4)^{k}	0.023
C(4)–O(10)	1.231 (3)^{i}	1.237 (4)^{i}	1.238 (5)^{i}	1.230 (6)^{l}	1.234 (8)	1.231 (4)^{l}	0.003
C(5)–C(11)	1.500 (3)	1.497 (4)	1.510 (5)	1.504 (8)	1.503 (13)	1.503 (4)	0.000
C(2)N(1)C(6)	121.1 (2)	120.6 (2)	120.4 (2)	121.8 (4)	121.0 (1.4)	122.8 (5)	1.8
C(2)N(1)C(7)	119.0 (1)	118.2 (2)	119.4 (2)	116.6 (4)	118.3 (2.8)		
C(6)N(1)C(7)	119.9 (2)	121.2 (2)	120.1 (2)	121.6 (3)	120.7 (1.7)		
N(1)C(2)N(3)	114.8 (2)	115.4 (2)	115.0 (2)	113.7 (4)	114.7 (1.7)	115.2 (5)	0.5
N(1)C(2)O(9)	123.4 (2)	123.3 (2)	124.3 (2)	124.3 (5)	123.8 (1.0)	122.7 (5)	1.1
N(3)C(2)O(9)	121.8 (2)	121.3 (2)	120.7 (2)	122.0 (4)	121.5 (1.3)	122.1 (5)	0.6
C(2)N(3)C(4)	127.0 (2)	126.3 (2)	126.3 (2)	127.5 (4)	126.8 (1.2)	126.3 (5)	0.5
N(3)C(4)C(5)	115.0 (2)	116.1 (2)	115.7 (2)	115.8 (4)	115.7 (1.1)	115.6 (5)	0.1
N(3)C(4)O(10)	120.4 (1)	120.0 (2)	119.9 (2)	119.7 (4)	120.0 (0.7)	118.3 (5)	1.7
C(5)C(4)O(10)	124.6 (2)	123.9 (2)	124.4 (2)	124.5 (5)	124.5 (0.7)	126.1 (5)	1.6
C(4)C(5)C(6)	118.0 (2)	118.3 (2)	119.0 (2)	117.2 (4)	118.1 (1.8)	118.2 (5)	0.1
C(4)C(5)C(11)	119.6 (1)	119.3 (2)	117.3 (2)	119.3 (4)	118.9 (2.3)	119.0 (5)	0.1
C(6)C(5)C(11)	122.4 (2)	122.4 (2)	123.6 (2)	123.5 (4)	123.0 (1.2)	122.8 (5)	0.2
C(5)C(6)N(1)	123.7 (2)	123.3 (2)	123.2 (2)	124.1 (4)	123.6 (0.9)	121.8 (5)	1.8

[a] The atom numbering in the various structures has been changed to conform to that used in the present analysis. No corrections for thermal motion have been made to obtain the dimensions used in this table. [b] Reference 13 [c] Reference 14; the values for the angles around N(1) given in a figure and in a table differ slightly in this paper. The latter are presented here. [d] Reference 17. [e] The average value for the dimension among the first four entries with the maximum discrepancy among these entries in parentheses (note, this figure is neither an estimated nor root mean square deviation). [f] Reference 15. [g] Difference between value for thymine monohydrate and the average of the first four columns. [h] This carbonyl bond is involved only in the possible C–H···O hydrogen bond. [i] Participates in an N–H···O hydrogen bond (2.83–2.88 Å). [j] Not involved in hydrogen bonding. [k] Participates in two N–H···O hydrogen bonds (2.83–2.84 Å). [l] Participates in an O–H···O hydrogen bond (2.74–2.84 Å).

as pointed out in the same survey, by far the most common packing mode for these pyrimidine derivatives is to have the C(4)–O(10) bond involved in a centrosymmetric pair of hydrogen bonds, so these results do not necessarily show that intermolecular effects are not responsible for the differences in these lengths. The bond lengths in the 1-methylthymine molecule and **1** (the two most accurately determined structures in Table III) are in very close agreement with the greatest difference being 0.014 Å ($\sim 3\sigma$) in the case of the C(4)–C(5) bond. When the comparison is extended to the bond angles, differences of greater than 1° (*i.e.*, $>5\sigma$) are quite common among the four N(1)-substituted thymine derivatives listed in Table III.

Molecular Geometry and Conformation of the Thymine Rings. Among these thymine derivatives, the molecule of **1** exhibits much the greatest deviation from planarity in the thymine ring. The deviations from the best plane through the six ring atoms range from −0.022 to 0.038 Å (Table IV), and the atoms C(7) and O(10)

Table IV. Some Details of Best Planes in the Molecule[a]

	N(1)	C(2)	N(3)	C(4)	C(5)	C(6)	C(7)	O(9)	O(10)	C(11)
Plane *A*[b]	*0.024*	*−0.011*	*−0.020*	*0.038*	*−0.014*	*−0.022*	0.144	−0.028	0.107	−0.024
Plane *B*	0.040	*0.005*	*−0.003*	0.056	*0.005*	*−0.005*	0.159	−0.014	0.126	−0.004
Equation of plane *A*[c]	$-0.955X + 0.058Y - 0.290Z + 0.566 = 0$									
χ^2 (plane *A*) = 541.7		$P^d \ll 0.005$								

[a] Atoms were weighted by $1/\sigma^2$, where σ is the standard deviation from the least-squares results. [b] Distances in italics are given for atoms included in plane calculations. [c] The orthogonal axes, X, Y, Z, have X along the a axis, Y in the ab plane, and Z along the c^* axis. [d] Probability that plane A is an accurate plane based on χ^2 test.

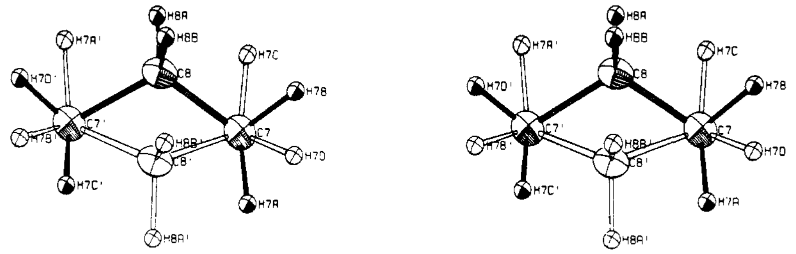
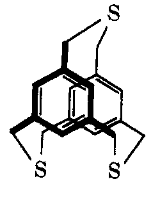


Figure 3. Stereoscopic view of the trimethylene bridge of 1 showing the nature of the disorder. The atoms and bonds for one of the ordered arrangements of molecules are distinguished by shading.

lie 0.144 and 0.107 Å from this plane. The conformation could be described as a "boat" with C(7), N(1), C(4), and O(10) lying 0.159, 0.040, 0.056, and 0.126 Å (toward the other thymine ring in the molecule) from the essentially exact plane through the atoms C(2), N(3), C(5), and C(6); the atoms O(9) and C(11) lie −0.014 and −0.004 Å from that plane. The greatest deviation of an atom from the plane through the ring atoms in the structures of 1-methylthymine, thymidine, and thymine monohydrate is 0.014 Å. The relatively large distortions of the thymine moiety in 1 are a consequence of the strains imposed upon this conformation of the molecule by the trimethylene bridge, and also possibly of the intermolecular overcrowding between the rings in the packing arrangement found in the crystal. Distances of substituent atoms of up to 0.34 Å from the planes of aromatic rings have been reported in ferrocene derivatives[20] and in cyclophanes.[21]

The conformation of the methyl group C(11) is such that one hydrogen atom, H(11A), lies almost in the plane of the ring but points away from O(10) (see Figure 2). The intramolecular H(11B)···O(10), H(11C)···O(10), and H(11B)···O(10′) distances are 2.85 (4), 2.98 (3), and 2.86 (3) Å, respectively. However, this arrangement for the methyl group leaves a hydrogen atom, H(11C), pointing toward the adjacent molecule, and in particular toward the C(4′)–O(10′) carbonyl group in the adjacent molecule, in the x direction. The intermolecular H(11C)···C(4′) and H(11C)···O(10′) distances are 2.87(3) and 2.89(3) Å. If this interaction is sufficiently strong, it could have the effect of forcing the carbonyl bond to point toward the C_2 axis through the center of the molecule thus tending to give the thymine ring a "boat" shape.

Disorder and Conformation of Trimethylene Bridges. There is crystallographic disorder around the C_2 axis in the neighborhood of the trimethylene bridge (Figure 3). Inspection of the thermal ellipsoids (Figure 2) does not suggest that the disorder persists beyond the positions for C(8), H(8A), H(8B), H(7A), H(7B), H(7C), and H(7D). Disorder around a C_2 axis was also found in other molecules with three-atom bridges, *e.g.*, in 2,11,20-trithia[3.3.3](1,3,5)cyclophane (**4**)[22] and



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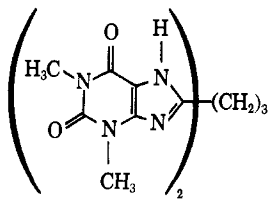

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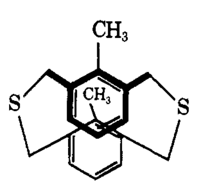

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in 8,8′-trimethylenebistheophylline (**5**),[23] although in the latter case the disorder also affects the carbon atom attached to the base. A related type of disorder, not required to be 1:1 by the presence of a symmetry element, was found by Davis and Bernal[24] in *syn*-2,11-dithia-9,18-dimethyl[3.3]metacyclophane (**6**), although in that case the two conformers constituting the crystallographic disorder are not equivalent. In the case of the crystal of **4**, convincing evidence was obtained for dynamic interconversion of the two chemically equivalent conformers that are related by the C_2 crystallographic axis, as the C_2 axis is lost at low temperatures.[22] The thermal ellipsoids found in the analysis of **1** imply that the principal molecular motion would be an oscillation about an axis perpendicular to the C_2 axis and parallel to the planes of the thymine rings. This is particularly true of C(8) and tends to suggest that a dynamic process of the type proposed in **4** does not take place here. The relative shortness of the C(7)–C(8) and C(7′)–C(8) bonds (1.496 (7) and 1.523 (7) Å) and the large value for the C(7)–C(8)–C(7′) angle (119.0 (2)°) imply considerable thermal motion as has been found in the case of other trimethylene groups.[25] At the temperatures (~20°) at which the

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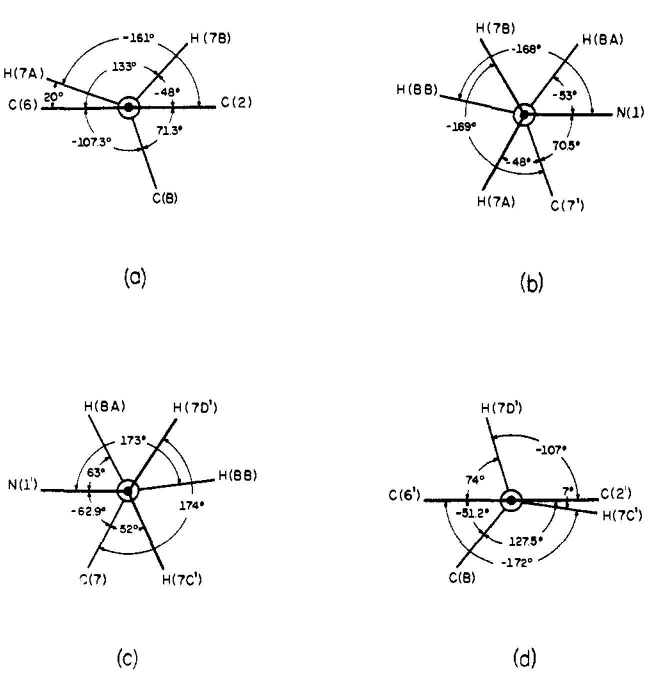

Figure 4. Torsion angles about (a) the N(1)–C(7), (b) the C(7)–C(8), (c) the C(7′)–C(8), and (d) the N(1′)–C(7′) bond. The angles are considered positive if the atom bonded to the closer atom has to be rotated clockwise to eclipse the atom bonded to the more distant atom.

crystals of **1** were examined, there was no evidence for additional reflections of the type detected in the study of **4**.[22] It is obvious, however, that such an effect would be smaller in the case of **1** as the dynamic process would affect mainly the position of a carbon rather than a sulfur atom as in **4**. As pointed out by Rosen and Hybl,[23] these disordered structures can be considered as a "form of twinning with the lattice containing those molecules of one persuasion being related to its sister lattice by a twin element (twofold axis)." In the present instance, the removal of the twofold axis would give rise to the space group $P2_1/c$ for an ordered arrangement of molecules of **1**. It is also possible to conceive of a structure for **1** having C_2 symmetry, with the C_2 axis passing through C(8), and yet retaining a fully staggered arrangement in the trimethylene bridge. However, in such a hypothetical case both the parallel arrangement and intramolecular overlap of the thymine rings would be lost.

The torsion angles in the trimethylene bridge portion of the molecule are shown in Figure 4. The arrangements of the carbon and nitrogen atoms around the C(7)–C(8) and C(7′)–C(8) bonds are gauche or skew with the C–C–C–N torsion angles (70.5 and 62.9°) being somewhat greater than those involving hydrogen atoms. In each molecule of **1**, a hydrogen atom on C(7) and C(7′) must lie close to the plane of a thymine moiety, in one case being close to H(6), in the other being close to O(9); the H(7A)···H(6) and H(7C′)···O(9′) distances are 2.08(5) and 2.20 (7) Å and the C(6)–N(1)–C(7)–H(7A) and C(2′)–N(1′)–C(7′)–H(7C′) torsion angles are 20 and 7°, respectively. In 1-methylthymine, two of the three hydrogen atoms were staggered with respect to O(9), suggesting that a possible conformer of **1** would have C_s symmetry with, in each ring, one of the hydrogen atoms of C(7) lying close to the plane of the thymine ring. This conformer may be destabilized by intramolecular overcrowding between the methyl groups on the two rings, or due to unfavorable packing patterns into which it can be accommodated. It is of interest that a conformation with approximate C_s symmetry was found for **1** to the extent of about 10% in the crystal of the cis–syn photodimer **2** of **1**,[4] where it was produced by the action of X-rays on the photodimer.

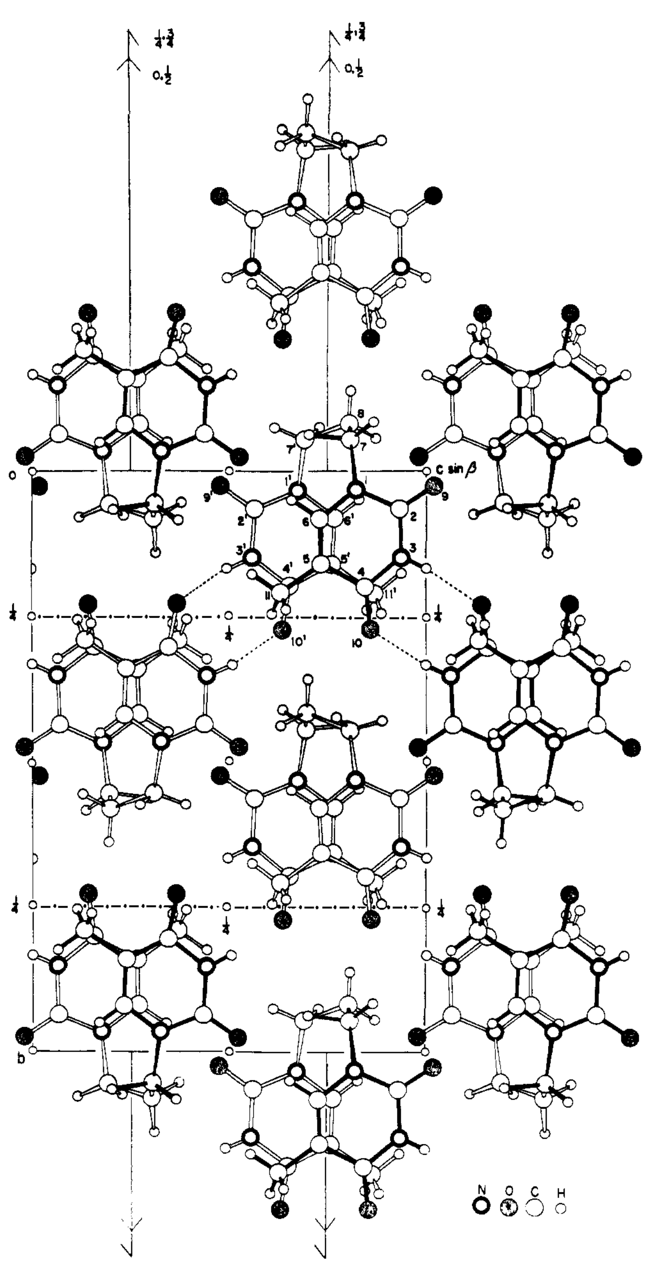

Figure 5. View of the packing in the unit cell looking along the *a* axis. The disorder of the trimethylene groups is not shown. The ordered arrangement of trimethylene groups in the various molecules that would correspond to $P2_1/c$ is given. The N–H···O hydrogen bonds are indicated for the basic molecule. It should be emphasized that the thymine rings are not quite perpendicular to the *a* axis so that the overlap of the rings as shown in this figure does not correspond to the projection of one on the other as discussed in a later section.

Crystal Packing and the Environment for the Solid State Reaction. Each thymine moiety forms a centrosymmetrical pair of N(3)–H···O(10) hydrogen bonds with a length 2.875 (2) Å to the thymine portion of another molecule (Figure 5). The N–H···O angle is

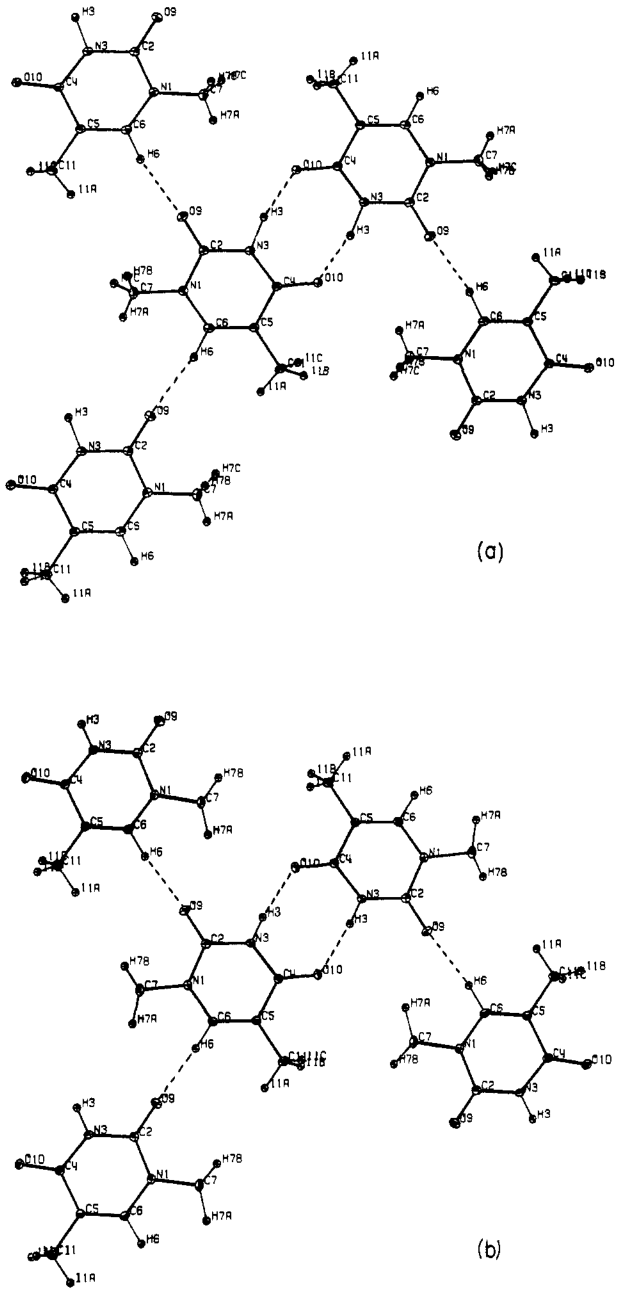

Figure 6. Suitably oriented views of the packing within layers of thymine molecules (a) in 1-methylthymine and (b) in **1**. The hydrogen bonds (including the C–H···O "interaction") have been marked. The atom numbering in 1-methylthymine has been changed to that used for **1** in the present paper.

172 (2)° and the H(3)···O(10) length is 1.98 (3) Å. On the basis of the survey by Voet and Rich,[19] this form of self-association, involving N(3) and O(10), is by far the most common among crystals containing only one species of a thymine or uracil molecule. The atoms N(3) and O(10) are those that form hydrogen bonds to adenine in the Watson–Crick scheme for DNA. Different arrangements, however, have been found in three more recently reported structures of thymine derivatives.[16–18] There is also a close contact of 3.169 (3) Å between C(6) and O(9) in another molecule. This interaction is in the direction of the C(6)–H(6) bond and results in an H···O contact of 2.20 (2) (Å); the C–H···O angle is 166 (2)°. Whether such an interaction is a hydrogen bond has been the subject of much discussion.[13,19,26–28] The geometry and apparently the nature of the interaction found here are almost identical with those found in the crystal of 1-methylthymine.[13] Indeed, the entire packing of **1** can be thought of as consisting mainly of layers of 1-methylthymine molecules (neglecting the central atom of the trimethylene bridges) and the structure of these layers is remarkably similar to the layers of 1-methylthymine molecules in that crystal (see Figure 6). Furthermore, the lengths of one of the crystallographic axes in the plane of the rings are almost equal in the two compounds; the *b* axis in 1-methylthymine is 12.091 (6) and the *c* axis in **1** is 12.067 (2) Å.

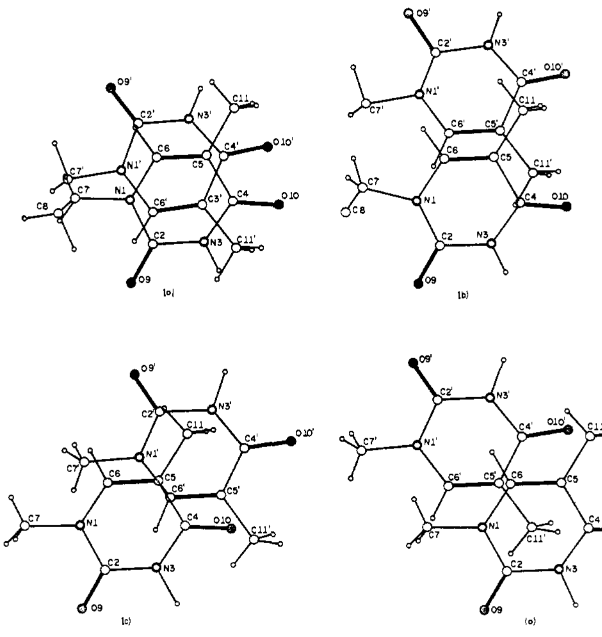

Figure 7. Projections of neighboring thymine rings onto the basic ring in the case of (a) intramolecular overlap in **1**, (b) intermolecular overlap in **1**, (c) overlap of the molecule at x, $\frac{1}{2} - y$, $-\frac{1}{2} + z$ on the basic molecule in 1-methylthymine, and (d) overlap of the molecule at x, $\frac{1}{2} - y$, $\frac{1}{2} + z$ on the basic molecule in 1-methylthymine.

There do not seem to be any particularly short contacts involving the hydrogen atoms of C(8) that might affect the position of C(8) with respect to the thymine rings.

The most significant feature of the crystal structure, however, is the intramolecular and intermolecular arrangement of the thymine rings. The molecules stack in columns along the *a* axis with these columns being cross-linked by the N–H···O and (possibly) C–H···O hydrogen bonds. These columns are nearly perpendicular to the planes of the thymine rings. The projection of one thymine ring onto the other in the same molecule is shown in Figure 7a. Upon irradiation in solution, **1** gives the cis–syn dimer **2**.[4] In the crystal, however, the thymine rings of **1** are so arranged that intramolecular cyclobutane ring formation upon uv irradiation would be expected to give the trans–syn dimer **3**. The intramolecular C(6)···C(6′) and C(5)···

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(28) C. A. Maier, J. A. Kapecki, and I. C. Paul, *J. Org. Chem.*, **36**, 1299 (1971).

Table V. Some Details of the Distance between Thymine Rings Involved in Photoreaction

	1		1-Methylthymine[a]	
	Intramolecular	Intermolecular		
C(5)···C(5′)	3.549 (3)	3.627 (3)	3.806 (4)	
C(6)···C(6′)	3.452 (4)	3.749 (4)	3.808 (4)	
C(5)···C(6′)	3.747 (3)	3.923 (3)	3.429 (4) 4.567 (4)[b]	
Shortest and longest distance of atom in adjacent ring from best plane through six ring atoms	2.977; N(1′) 3.285; C(4′)	3.539; C(4′) 3.846; N(1′)	3.030; C(2′) 3.398; C(5′)	3.370; C(5′)[c] 3.738; C(2′)
Distance of C(5′) and C(6′) in adjacent ring from best plane through six ring atoms	C(5′) 3.263 C(6′) 3.115	3.561 3.707	3.398 3.390	3.370 3.378
Angle between planes of two adjacent thymine rings	6° 38′		8° 47′	

[a] Dimensions calculated by us from data in ref 13. In the abstract of ref 13, the length of the *a* axis is given as 7.531, while in the main text it is given as 7.351 Å; the latter value is clearly correct. [b] In this case the symmetry operations are such that there are two independent C(5)···C(6′) distances. [c] There are two different projections of adjacent molecules in the case of 1-methylthymine. While the atom–atom distances are the same, the atom–plane distances are different.

C(5′) distances are 3.452 (4) and 3.549 (3) Å, and the distance between the midpoints of the double bonds is 3.501 Å. The distances between these double bonds conform to the criteria proposed by Schmidt[29] for a photochemical reaction to occur under topochemical control. The intramolecular distance between the thymine rings in **1** is clearly comparable to the distance between adjacent thymine residues in DNA, where, however, the arrangement of the molecules is such as to give the cis–syn dimer upon irradiation.

As can be appreciated from Figure 2, the crystal structure of **1** would also permit intermolecular as well as intramolecular photochemical reaction. The C(5)=C(6) double bonds of thymine rings in adjacent molecules in the *x* direction are also close to each other; the intermolecular C(5)···C(5′) and C(6)···C(6′) distances are 3.627 (3) and 3.749 (4) Å, respectively, while the distance between the midpoints of the double bonds is 3.688 Å. The projection of the thymine ring onto its intermolecular neighbor is shown in Figure 7b. This latter arrangement of molecules would predetermine the formation of a polymer containing cyclobutane rings with the trans–syn geometry as the crystal consists of stacks of molecules so oriented along the *a* axis. Photochemical formation of a high molecular weight linear polymer from crystalline 2,5-distyrylpyrazines and from crystalline 1,4-bis[β-pyridyl-(2)-vinyl]benzene has been reported by Hasegawa and coworkers.[30] In those cases, the polymerization reaction was shown to exhibit topotaxy.[30] As reported in the preceding paper,[5] the photoreaction of **1** in the solid state gives a polymeric product having cyclobutane rings with the trans–syn geometry. While comments on the mechanism of polymerization must remain speculative, the tendency for polymerization over dimerization may be due in part to a cooperative effect within a column of molecules, much like the action of a zip fastener.

There have been previous correlations of the stereochemistry of the thymine dimers formed by irradiation of single crystals[31] and of frozen solutions[32] with the structures found in the crystal for anhydrous and hydrated thymines. In 1-methylthymine, the center–center distance of the double bonds in the closest pair of molecules in adjacent sheets of the type shown in Figure 6b is 3.807 Å.[13] Stewart[31] discovered that upon uv irradiation of a single crystal of 1-methylthymine, a photodimer was produced which has been shown to have the trans–syn geometry,[33] a result which he predicted from the crystal structure. The present case, however, is the first example in the thymine series where polymer formation would be possible.

In view of the tendency for polymer formation,[5] it is of interest to examine the geometric relationships between the thymine rings in **1** that would lead to both inter- and intramolecular reaction. In the molecule of **1**, the best planes through the two thymine rings are inclined to each other at an angle of 6° 38′ and the shortest intramolecular distances involving C(5) and C(6) are C(5)···C(4′) and C(6)···N(1′) at 3.331 (3) and 3.167(3) Å, respectively. From Figure 7a, it can be seen that the projection of a thymine ring onto its intramolecular neighbor results in very substantial overlap. While the C(5) and C(6) atoms are within 3.6 Å of C(5′) and C(6′), respectively, they lie almost exactly over the N(1′)–C(4′) vector. In contrast, there is no ring–ring overlap between intermolecular neighbors (Figure 7b), but the C(5)–C(6) and C(5′)–C(6′) bonds are close to being overlapped and constitute the shortest ring–ring distances between adjacent molecules in the *a* direction. Although the individual C(5)···C(5′) and C(6)···C(6′) distances are slightly longer than in the intramolecular case (Table V), it is reasonable to assume that there is a closer interaction of the π-electron orbitals of the two double bonds in Figure 7b than in 7a. The photochemical process, which intimately involves the π electrons, will thus be enhanced between thymine rings in different molecules.

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It should be pointed out that the present structure corresponds to the rare case which has the potential reacting centers related by C_2 symmetry. Virtually all the examples discussed by Schmidt[29,34] have the reactant molecules related by C_1 (leading to a product with C_s symmetry) or by C_i symmetry (leading to a product with C_i symmetry). Unlike the cases of C_1 and C_i symmetry, the double bonds in the reactant molecules are not required to be parallel when the molecules are related by C_2 symmetry. Schmidt[34] has indicated one case, that of methyl *m*-bromocinnamate,[35] where nonparallelism of double bonds prevents reaction. In the crystal of methyl *m*-bromocinnamate, one of the potentially reactant double bonds makes an angle of 28° with the other when projected along the line joining the centers of the two bonds; the centers of the bonds are 3.93 Å apart. In the crystal of Thy-C_3-Thy, the corresponding projection angle is 5° when considering the C(5)–C(6) double bonds within the molecule and 4° when considering those between two adjacent molecules.

For comparison, the projections of the two adjacent molecules on the basic molecule in the 1-methylthymine crystal[13] are shown in Figures 7c and 7d. In one case (Figure 7c), the overlap of the molecule related by a glide plane at $x, {}^1/_2 - y, -{}^1/_2 + z$ over the one at x, y, z, C(6′) lies along the C(5)–C(6) bond and the C(5)···C(6′) distance (3.429 (4) Å) is much shorter than the C(5)···C(5′) or C(6)···C(6′) distances (3.806 (4) and 3.808 (4) Å, respectively). As pointed out by Stewart,[31] topochemical considerations dictate formation of the trans–syn dimer. The overlap of the molecule at $x, {}^1/_2 - y, {}^1/_2 + z$ on that at x, y, z in 1-methylthymine is shown in Figure 7d. There is no inter-ring overlap but the projected C(5′)–C(6′) bond is almost an extension of C(5)–C(6). The C(6)···C(5′), C(6)···C(6′), and C(5)···C(5′) distances are as given in the case of Figure 7c. In 1-methylthymine, the double bonds are only 1° from parallelism in both potentially reactive sites. In both geometries for the 1-methylthymine reactions, there will be greater interpenetration of the π orbitals of the two C═C double bonds than in the intramolecular geometry for Thy-C_3-Thy.

From the above arguments, *it appears that a short C···C distance between reacting carbon atoms is not necessarily the most important factor in permitting photochemical reactions and that in appropriate cases, the orientation of the participating orbitals may be a more important factor in determining the process.*

An additional factor which might have some effect in determining the course of the reaction is the disposition of the atoms in the thymine moiety about the best plane through C(2), N(3), C(5), and C(6). As described earlier, the deviations of the atoms C(7), N(1), C(4), O(9), and O(10) are all in the direction of the other thymine ring in the molecule. It is possible that the position of these atoms might offer a slight barrier to a closer approach of the two rings for intramolecular reaction. However, we consider the relative orientation of the two rings as being more important in the determination of the course of the reaction.

Several aspects of this process deserve further study. It would be of interest to investigate whether the polymerization exhibits topotaxy and also whether solid state reactions occur in other Thy(1(CH_2)$_n$1)Thy and Ura(1(CH_2)$_n$1)Ura crystals.

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