about C(2')—O(2') which is only −0·6°. The pseudorotation parameters for the dioxolane ring are $P = 124°$, $\lambda_{m,\max} = 33·9°$ (Sprang, Rohrer & Sundaralingam, 1978). This value is close to that of the dioxolane ring in MMU (32·3°).

The conformation about the exocyclic C(4')—C(5') bond is *gauche–gauche* with the torsion angles $\varphi_{OO} = -68·4$ and $\varphi_{OC} = 51·3°$.

Molecular packing

The packing of the molecules in the unit cell is shown viewed down *c* and *a* in Figs. 4 and 5 respectively. The molecules run in a helical fashion parallel to *c*. This is stabilized by the intermolecular hydrogen bond N(3)—H···O(2) (2·906 Å). Neighbouring helical columns are linked through the other hydrogen bond O(4)···H—O(5') (2·720 Å). These are the only hydrogen bonds in the extended crystal structure.

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The *trans-anti* Photodimer of 1-Methylthymine: Direct Evidence of X-ray Cleavage of Dimer into Monomers in the Crystalline State*

BY CHIN HSUAN WEI AND J. RALPH EINSTEIN

Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37830, *USA*

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Abstract

The title compound, $(C_6H_8N_2O_2)_2$, is monoclinic, $P2_1/c$, with $a = 7·5420$ (3), $b = 6·2277$ (2), $c = 14·4633$ (5) Å, $\beta = 117·039$ (3)°, $Z = 2$. Other pertinent information: $D_x = 1·538$ Mg m^{-3}, $U = 605·08$ Å^3, $F(000) = 296$, μ(Cu $K\alpha$) = 1·0026 mm^{-1}, transmission = 0·800–0·922, $T = 297$ K. The structure was solved by direct methods. Refinement yielded $R(F) = 0·039$ for 1052 nonzero counter data to 0·84 Å. The dimer is of the *trans-anti* type, having a crystallographic center of symmetry at the center of its cyclobutane ring. The pyrimidine ring is folded along the N(1)···C(4) line with a dihedral angle of 163·6 (1)° between two planes each consisting of four ring atoms. About 4% of the molecules exist in the monomeric form, presumably because of prolonged X-irradiation. E.s.d.'s of bond lengths and angles involving C, N, O atoms are 0·002 Å and 0·1°. Through pairs of centrosymmetrically related N(3)H···O(2) hydrogen bonds, the dimers form infinite chains in the [1$\bar{1}$0] direction.

Introduction

When frozen solutions of pyrimidines or *N*-methylated pyrimidines are irradiated by UV light, dimerization across the 5,6-double bonds takes place. Depending on the geometrical arrangement of pyrimidines with respect to the cyclobutane ring thus formed, and on the type of 5,6 : 5',6' linkage for the two pyrimidines, it was proposed that four different stereoisomers could be

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formed, *viz*., *cis-syn*, *cis-anti*, *trans-syn*, and *trans-anti* types (Wulff & Fraenkel, 1961). Subsequently, between 1968 and 1972, structural determinations of 10 photodimers of the four types were carried out (for a review, see Karle, 1976). Among them, the *cis-syn* type that occurs in DNA (Weinblum & Johns, 1966) was the most prevalent, and structures of only two dimers of the *trans-anti* type, those of thymine (Camerman & Nyburg, 1969) and 1-methylthymine (Einstein, Hosszu, Longworth, Rahn & Wei, 1967), were reported. (The latter was a preliminary account of part of the work described here.)

The cyclobutane ring of thymine photodimers has long been recognized as being susceptible to cleavage in solution, yielding monomers by UV light (Beukers & Berends, 1960) and X-rays (Lochmann, 1963). Even in the solid state monomerization can take place, as determined by optical methods, for crystals of all four stereoisomers of dimethylthymine dimer irradiated with ^{60}Co γ-rays (Weinblum, 1969). Evidence of monomerization from X-ray structural studies has so far been reported for three crystals of the *cis-syn* type. In the structure of 1,1′-trimethylene-linked thymine dimer (Leonard, Golankiewicz, McCredie, Johnson & Paul, 1969) four monomeric sites, corresponding to cyclobutane-ring atoms, were located, and were subsequently included in the refinement (each with 10% occupancy). Although monomerization was strongly suspected in the structure of 1,3-dimethylthymine dimer (Camerman & Camerman, 1970) because one of the inter-pyrimidine bonds was unrealistically long (1·66 Å), the authors were not able to find evidence of monomer sites. The third case was the sodium salt of thymine dimer (Wei & Einstein, 1968), for which the sites of all nonhydrogen monomer atoms were located.

We present here details of our recent structural reinvestigation of 1-methylthymine photodimer, including newly found evidence of the coexistence of monomeric species in the crystalline state, and refinement of a mixed dimer–monomer model. The results confirmed that X-ray splitting of a *trans-anti* photodimer can indeed occur, as in the case of dimethylthymine dimer (Weinblum, 1969). The results also provide further information regarding the pyrimidine-ring conformation when the cyclobutane ring is planar.

Experimental

The sample was prepared by UV irradiation (254 nm) of frozen solutions of 1-methylthymine. The unreacted monomeric species was removed from the dried residue by repeated washing with cold ethanol in which the photoproduct is insoluble. Crystals of the dimer were grown from aqueous solution at 277 K. After preliminary Weissenberg and precession photographs were taken, the cell parameters were refined by the least-squares method using 11 strong reflections in the 2θ range of 118–132° on an Oak Ridge computer-controlled diffractometer (Busing, Ellison, Levy, King & Roseberry, 1968). Intensity data were then collected from a crystal of size 0·09 × 0·17 × 0·36 mm, up to a 2θ value of 133° using Cu $K\alpha$ radiation.† Data collected by ω-step scans ($2\theta < 60°$) were merged with those collected by θ–2θ step scans. Thus, intensities of 1052 unique, nonzero reflections were obtained. They were corrected for absorption and assigned weights for least-squares refinement in the manner given elsewhere (Wei & Einstein, 1978).

Solution and refinement of the structure

The structure was solved by the symbolic addition procedure with the use of the program *MAGIC* (Fleischer, Stone & Dewar, 1966). After parameters of 10 independent nonhydrogen atoms were refined with the program *ORFLS* (Busing, Martin & Levy, 1962), a difference Fourier map showed all eight independent H atoms. The refinement (based on F^2) in which an isotropic-extinction parameter (Coppens & Hamilton, 1970) was included, and in which thermal parameters of the nonhydrogen atoms were treated anisotropically and those of the H atoms isotropically, converged to give $R(F)$ and $R(F^2)$ values of 0·050 and 0·070. $R_w(F^2)$, defined as $(\sum w|F_o^2 - sF_c^2|^2/\sum wF_o^4)^{1/2}$, where s is a scale factor, was 0·132. All molecular parameters calculated by the use of the program *ORFFE* (Busing, Martin & Levy, 1964) appeared normal.

A difference Fourier map calculated at this stage contained five residual peaks with densities (0·3 to 0·5 e Å^{-3}) somewhat higher than the expected noise level. Model building revealed that the seven highest peaks (0·2 to 0·5 e Å^{-3}) of the difference Fourier map were roughly coplanar, with a configuration suggesting seven of the 10 heavy-atom positions of a 1-methylthymine molecule, such as might have resulted from X-ray splitting of the dimers. The dimer atom C(2) and another difference Fourier peak [N(3*)] corresponded reasonably well in position to two of the three remaining atoms of the monomer. Refinement was continued with a mixed dimer–monomer model, with the monomer atoms fixed at the difference-Fourier-map positions, and their thermal parameters fixed as 2 Å^2 for ring atoms, 3 Å^2 for exocyclic atoms. The dimer atoms were constrained to have the occupancy m, except for C(2), an average site, for which the occupancy was 1, and the corresponding monomer atoms (only C, N, O atoms) were given the occupancy

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† About two days after data collection was initiated, an electronic noise problem arose. After it had been solved, the whole set of data was recollected. The total estimated exposure for the crystal was nine days at 35 kV and 20 mA.

Table 1. *Positional parameters* [C, N, O, $\times 10^4$; H *and minor monomeric sites* (*with asterisks*), $\times 10^3$] *and equivalent isotropic* (C, N, O) *or isotropic* (H) *thermal parameters* (Å^2)

The e.s.d.'s of the least significant figures are given in parentheses. Equivalent isotropic thermal parameters were calculated according to Hamilton (1959).

	x	y	z	B_{eq} or B
N(1)	1552 (2)	395 (2)	4205 (1)	2·2
C(2)	979 (2)	2208 (2)	4509 (1)	2·3
N(3)	2460 (2)	3399 (2)	5293 (1)	2·3
C(4)	4457 (2)	2982 (2)	5783 (1)	2·2
C(5)	5057 (2)	705 (2)	5705 (1)	2·1
C(6)	3485 (2)	−590 (2)	4793 (1)	2·0
C(7)	43 (3)	−905 (3)	3383 (1)	3·0
C(8)	5730 (3)	−371 (3)	6764 (1)	2·9
O(2)	−745 (2)	2866 (2)	4122 (1)	3·1
O(4)	5665 (2)	4344 (2)	6277 (1)	3·2
H(3)	198 (3)	466 (4)	543 (2)	3·4 (4)
H(6)	322 (3)	−206 (3)	497 (1)	2·2 (3)
H(7*a*)	54 (4)	−136 (5)	291 (2)	6·8 (7)
H(7*b*)	−10 (5)	−236 (6)	364 (3)	7·9 (8)
H(7*c*)	−101 (4)	−13 (5)	303 (2)	5·6 (6)
H(8*a*)	451 (4)	−56 (4)	686 (2)	4·5 (5)
H(8*b*)	631 (3)	−179 (4)	673 (2)	3·6 (4)
H(8*c*)	683 (4)	47 (4)	737 (2)	4·5 (5)
N(1*)	114	40	437	(*a*)
N(3*)	218	362	538	(*a*)
C(4*)	358	263	590	(*a*)
C(5*)	425	35	603	(*a*)
C(6*)	281	−42	548	(*a*)
C(7*)	−104	−114	354	(*b*)
C(8*)	637	−24	643	(*b*)
O(2*)	−59	302	383	(*b*)
O(4*)	510	385	657	(*b*)

(*a*) Assigned 2·0 Å^2. (*b*) Assigned 3·0 Å^2.

$1 - m$. After further least-squares cycles, eight monomer atomic positions were re-established from the eight highest peaks of a partial difference Fourier map. Another peak with considerably lower density was assigned as the tenth monomer atom [C(6*)], and the refinement was continued in the same manner. At convergence, the parameter shifts were all less than 2% of the corresponding e.s.d.'s. The $R(F)$, $R(F^2)$, and $R_w(F^2)$ values stood at 0·039, 0·053, and 0·106, respectively; the value of m was 0·964 (2), and that of the isotropic-extinction parameter was 0·014 (3). The scattering factors used were those of Berghuis, Haanappel, Potters, Loopstra, MacGillavry & Veenendaal (1955) for C, N, and O; those of Stewart, Davidson & Simpson (1965) were used for H. The final atomic parameters are given in Table 1.†

Discussion

The 1-methylthymine dimer has a crystallographic center of symmetry at the center of its cyclobutane ring. A stereoscopic view of the dimer is shown in Fig. 1, and interatomic bond distances and bond angles are given in Fig. 2. These values are not significantly different from those obtained on refinement of the dimer alone (without partially occupied monomer sites). The largest difference in the bond distances on changing to the final, mixed dimer–monomer model was an increase of 0·005 Å for N(1)–C(2); the average difference for bond lengths between nonhydrogen atoms was 0·002 Å.

The dimer bond distances and angles are less reliable than as indicated by their e.s.d.'s, because of the disorder. Still, they fall within the ranges tabulated for pyrimidine photodimers (Karle, 1976). The N(1)–C(2) distance is 0·017 Å longer, and the C(6)–N(1)–C(2) angle is 2·4° smaller, than the corresponding values observed for the thymine *trans-anti* photodimer (Camerman & Nyburg, 1969).

The cyclobutane ring is planar by symmetry. The pyrimidine ring is folded along the N(1)···C(4) line

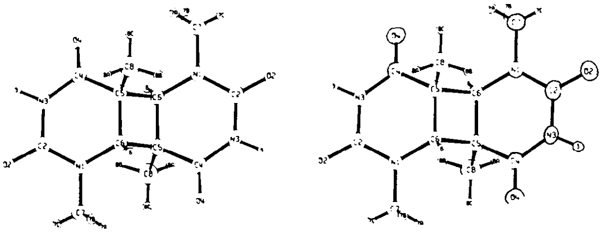

Fig. 1. A stereoscopic view of the *trans-anti* photodimer of 1-methylthymine. All figures were prepared by the use of the program *ORTEP*-II (Johnson, 1976).

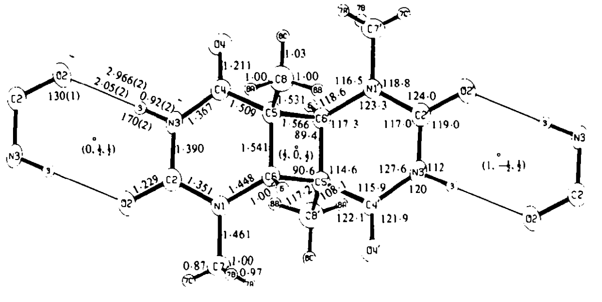

Fig. 2. Bond lengths (Å) and bond angles (°) for the dimer molecule and hydrogen-bond parameters. Primes refer to atoms related to those in the asymmetric unit by the crystallographic center of symmetry. The angles C(8)–C(5)–C(6) and C(6)–C(5')–C(4') are 113·8 and 112·0°, respectively. Not shown are 15 bond angles involving H atoms attached to tetrahedral carbons. They range from 98° for H(7*a*)–C(7)–H(7*b*) to 120° for H(7*b*)–C(7)–H(7*c*), with an average value of 109·7°. E.s.d.'s are as follows, where X denotes a nonhydrogen atom: for bond lengths X–X, 0·002, X–H, 0·01–0·03 Å [single exception, 0·04 Å for C(7)–H(7*b*)]; for bond angles X–X–X, 0·1, H–X–X, 1–2, H–X–H, 2° [single exception, 3° for H(7*a*)–C(7)–H(7*b*)].

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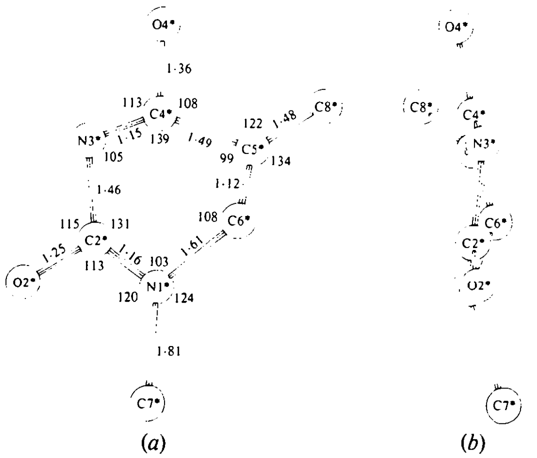
† Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35711 (4 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

with C(5) and C(6) atoms out of the best plane formed by N(1), C(2), N(3), and C(4) by 0·423 (3) and 0·322 (3) Å in the same direction. A similar folded configuration has been observed for one of the two pyrimidine rings in 1,1′-trimethylene-linked thymine *cis-syn* photodimer (Leonard *et al.*, 1969), in which C(5) and C(6) atoms are out of the best plane formed by the remaining four pyrimidine-ring atoms by 0·30 and 0·32 Å. Another folded configuration was found in one of the two pyrimidine rings of 6-methyluracil *cis-syn* photodimer (Gibson & Karle, 1971), in which the folding of 11·5 ° is along the N(3)···C(6) line.

It was stated by Karle (1976) that when the cyclobutyl ring is planar, or nearly so, the adjacent six-membered rings are also planar. This generalization holds for one of the two pyrimidine rings in the structure of Leonard *et al.* (1969), for *trans-anti* thymine dimer (Camerman & Nyburg, 1969), and for one pyrimidine ring adjacent to the cyclobutane ring in a thymine trimer (Flippen & Karle, 1971). However, the folded conformation for the other pyrimidine ring in the structure cited above of Leonard *et al.* (1969) is a counter-example to this generalization. The folded conformation, observed in the present structure, provides an additional counter-example.

In the present structure, the group of atoms on one side of the fold, N(1), C(2), N(3), and C(4), are coplanar to within 0·007 Å (plane 1). The group on the other side of the fold, N(1), C(6), C(5), and C(4), are much less coplanar, with a maximum deviation of 0·04 Å from the least-squares plane (plane 2). The dihedral angles between various planes are: planes 1 and 2, 163·6 (1)°; plane 2 and cyclobutane ring, 118·2 (1)°; plane 1 and cyclobutane ring, 134·5 (1)°. The torsion angles C(4)—C(5)—C(6)—C(5′) and N(1)—C(6)—C(5)—C(6′) are 114·6 (1) and −122·2 (2)°, respectively.

The 1-methylthymine dimers are connected in infinite chains along the $[1\bar{1}0]$ or $[\bar{1}10]$ directions by centrosymmetrically related pairs of N(3)H···O(2) hydrogen bonds (Fig. 2). This type of hydrogen bonding occurs very frequently in the crystals of photodimers reviewed by Karle (1976). O(4) atoms do not participate in hydrogen bonding. Excluding N(3) and O(2) atoms, the shortest intermolecular (dimer) contact between nonhydrogen atoms is 3·38 Å for O(4)···C(4), and that between nonhydrogen and H atoms is 2·48 Å for O(4)···H(8*b*).



(*a*) (*b*)

Fig. 3. (*a*) The framework of monomer atomic sites, as obtained from a partial difference Fourier map. (*b*) A view rotated 90° clockwise around the N(1*)···C(4*) direction.

The coordinates of monomer atomic sites, as obtained from a partial difference Fourier map, are included in Table 1, and the observed monomer configuration is shown in Fig. 3. Although these atomic sites roughly conform to those for the 1-methylthymine framework, their occupancy is low (only 3·6%), and these sites were not refined, except for their occupancy. The splitting of dimer into monomers in the crystalline state upon X-irradiation has previously been reported only for three *cis-syn* isomers (see *Introduction*). The case of the sodium salt of thymine dimer (Wei & Einstein, 1968), in which extensive remonomerization resulted in a dimer–monomer ratio of roughly 7:3, is the only one for which a complete model for the disorder, including all nonhydrogen atoms of the monomers, has been successfully refined (J. R. Einstein & C. H. Wei, to be published).

Despite the fact that in this *trans-anti* dimer there is no strain created by the crowding of methyl groups attached to C(5) and C(5′), as in the three *cis-syn* cases cited above, our results show that X-rays can result in sufficient monomerization for detection in a structural study, though less than in the above cases. This finding is in accordance with the observations of Weinblum (1969) that γ-rays monomerize the three 'unstrained' stereoisomers of dimethylthymine photodimer, besides the strained *cis-syn* type.

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Structure du Benzoyl-1 *n*-Butyl-2 Phénacylidène-3 Tétrahydro-1,2,3,4 Quinoxaline

PAR B. VIOSSAT

Laboratoire de Chimie Minérale, UER de Médecine et de Pharmacie, 34 *rue du Jardin des Plantes,*
86034 *Poitiers CEDEX, France*

N. RODIER

Laboratoire de Chimie Minérale, Faculté des Sciences Pharmaceutiques et Biologiques, rue J.-B. Clément,
92290 *Châtenay-Malabry, France*

ET Y. METTEY ET J.-M. VIERFOND

Laboratoire de Chimie Organique, UER de Médicine et de Pharmacie, 34 *rue du Jardin des Plantes,*
86034 *Poitiers CEDEX, France*

(*Reçu le* 10 *janvier* 1980, *accepté le* 22 *septembre* 1980)

Abstract

Crystalline $C_{27}H_{26}N_2O_2$ is monoclinic, space group $P2_1/b$, with $a = 11{\cdot}335\,(3)$, $b = 13{\cdot}012\,(2)$, $c = 15{\cdot}513\,(6)$ Å, $\gamma = 98{\cdot}56\,(3)^\circ$, $Z = 4$, $D_m = 1{\cdot}22\,(1)$ and $D_x = 1{\cdot}204$ Mg m^{-3}. Data were collected on an Enraf–Nonius CAD-4 diffractometer using Mo $K\alpha$ radiation. The crystal structure was solved by direct methods and refined by full-matrix least-squares analysis to a final R of 0·055 for 1784 independent reflections. All the H atoms, except those attached to the last two C atoms of the butyl group, were located and refined. The crystal structure can be regarded as consisting of either layers parallel to the (120) plane or columns built along 2_1 axes parallel to Oz in the (100) plane. An intramolecular N—H···O hydrogen bond forms a pseudo-ring in which four bonds are involved with non-located π electrons. The interatomic distances and bond angles are in good agreement with values reported in the literature.

Introduction

La préparation du benzoyl-1 *n*-butyl-2 phénacylidène-3 tétrahydro-1,2,3,4 quinoxaline a été réalisée dans le cadre de la recherche de molécules susceptibles de présenter une action anti-inflammatoire. Les méthodes

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