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E.H.M.O. Calculations on the Actual Conformations of Thymine Photodimers

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Extended Hückel molecular orbital calculations have been carried out on the actual structures of some photodimers of uracil and thymine. The results are compared with those derived for some postulated models by Jordan and Pullman, and the differences between the real structures and the models are examined.

Introduction

In a recent paper, Jordan and Pullman (JP) [1] gave the results of extended Hückel molecular orbital (E.H.M.O.) calculations on a number of assumed conformations of uracil and thymine photodimers, and, for various isomers, concluded from the total orbital energies which of the possible postulated structures would be the most stable. The actual molecular conformations of two thymine photodimers had been established by accurate X-ray structure determinations [2, 3], but use was not made of this information by JP; we assume that they were unaware of these results. In any event, it would now be of value to compare the results and predictions given by JP with the results of E.H.M.O. calculations on the known conformations of these photodimers. In addition to the structural determinations cited above, a number of other photodimer isomers have recently been studied by X-ray diffraction [4, 5, 6], and we submit here the results of E.H.M.O. calculations on those isomers where comparison is possible with the results of JP.

Method of Calculation

The program employed for the E.H.M.O. calculations was one which originated from Hoffmann [7], somewhat modified for local use by Professor I. G. Csizmadia. The Slater orbital exponents, diagonal matrix elements, and the K coefficient in the Wolfsberg-Helmholtz formula for the off-diagonal matrix elements were the same as those used by JP [8]. Thus the results should be readily comparable.

Results and Discussion

1. Cis-Syn Uracil Dimer (Fig. 1a)

The true structure gives a total orbital energy 34.75 kcal/mole lower than the "most stable" conformation derived by JP (Table). It is interesting to note that while the JP calculations indicated that for all the dimers "the most stable con-

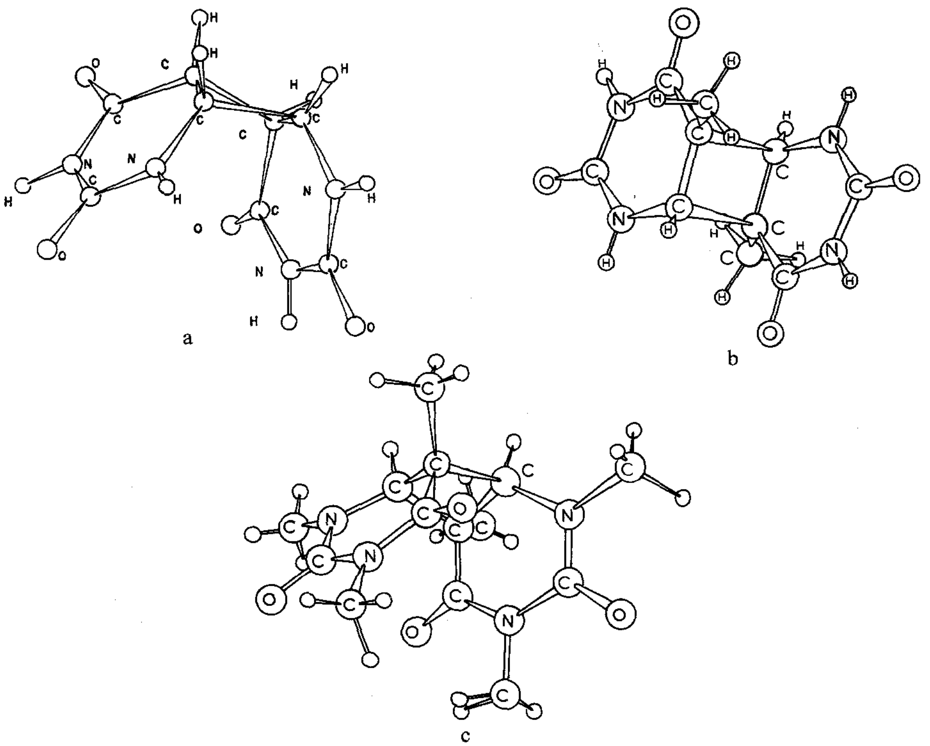

Fig. 1. Actual structures of (a) *cis-syn* uracil photodimer, (b) *trans-anti* thymine photodimer, (c) *cis-anti* 1,3-dimethylthymine photodimer

formations are obtained with planar bases" and "the least stable (by about 80–100 kcal/mole) are those derived from the half-chair model", the bases in this uracil photodimer are actually in the half-chair conformation: C5 and C6 are −0.13 Å and +0.15 Å out of the best plane through the other four atoms of the heterocycle nucleus [6].

2. *Trans-Anti Thymine Dimer (Fig. 1b)*

The total orbital energy calculated for the true structure is 26.17 kcal/mole less than that of the best JP conformation. The bases (omitting the methyl groups) are relatively planar, as was concluded in the JP model, the maximum deviation from planarity being 0.06 Å.

Table. *Total orbital energies of photodimers (kcal/mole)*

Dimer	a) This work (E)	b) Ref. [1] (E_{JP})	Difference a) − b)
Uracil, *cis-syn*	−38867.62	−38832.87	−34.75
Thymine, *trans-anti*	−43668.71	−43642.54	−26.17
Thymine, *cis-anti*[a]	−43631.99[b]	−43643.93	+11.94

[a] This structure not known: this result was obtained by replacing the methyl groups in the same isomer of 1,3-dimethylthymine photodimer [5], by hydrogens at appropriate distances.

[b] Total orbital energy calculated for the *cis-anti* photodimer of 1,3-dimethylthymine is −53205.88 kcal/mole.

3. Cis-Anti Thymine Dimer (Fig. 1c)

A structure for this dimer was derived for comparative purposes by substituting hydrogens in place of methyl groups in the known structure of the *cis-anti* photodimer of dimethylthymine [5]. The energy calculated for this structure is similar (12 kcal/mole higher) to that of the best conformation of JP. In the JP model the bases were planar; in this structure C6 lies 0.4 Å out of the plane of the other heterocycle-nucleus atoms in both bases.

In addition to their conclusion that planar bases give the most stable structures, JP also concluded that the most stable conformation for all of the photodimers had an angle of 120° between the planes of the bases and the cyclobutane plane. This conclusion was predicated, of course, on the assumption of a planar cyclobutane ring in each photodimer; in reality the cyclobutane in the crystal structures in all of the *cis* uracil and thymine photodimers so far elucidated is markedly puckered (dihedral angles of 153–155°), and it is therefore difficult to calculate a cyclobutane-base angle. However, if one calculates the angles between the "best plane" through the four atoms of the cyclobutane rings and the planar portions of the bases, values of 110–115° are obtained. In the *trans-anti* thymine photodimer the cyclobutane is necessarily planar in the crystal because the space-group requires a molecular centre of symmetry, and the base-cyclobutane angle is 113.7°. In addition to the planarity of the cyclobutanes (and as a consequence of this planarity), JP have used models in which the ring atoms of the two bases are in positions of maximum conflict (that is, atoms in one pyrimidine ring are directly opposite atoms in the other); in reality, in the *cis* photodimers the bases are twisted away from such conflict by 24–29°.

Clearly, the main conclusion to be drawn from this work is that these molecular-orbital calculations are useful in predicting probable structures only if all *likely conformations* have been tested.

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