mediate or rate-determining nucleophilic attack on this intermediate.[10,11,22]

For rate-determining formation of the first ion pair the α-D effect should be dependent on leaving group[19] and substrate reactivity;[16,24] for rate-determining nucleophilic attack on an ion pair the isotope effect should in addition be dependent on solvent nucleophilicity.[24] Intermediate mechanisms are hard to isolate experimentally so some but not all of these expectations have been experimentally verified. The "partitioning isotope effects" observed by Murr and Donnelly[25] provide a striking independent confirmation of the difference in isotope effects between processes with k_1 rate determining and those with k_2 rate determining.

Because of the interest in the mechanism of solvolysis of adamantyl derivatives and the suggestion that 2-adamantyl toluenesulfonate solvolyzes by a nonnucleophilic mechanism,[26a-e] we thought it would be of interest to examine the α-D effects on solvolysis of a 2-adamantyl derivative. One problem which presented itself was that with the usual leaving groups the low reactivity of the compounds requires that solvolysis be done either at elevated temperatures or in strongly acidic solvents. Since we have not yet demonstrated that we can measure rates with the required accuracy, better than $\pm 1\%$, under any of these conditions, we chose a more reactive sulfonate leaving group, 2,2,2-trifluoroethylsulfonate ("tresylate").[27,28]

2-Adamantyl tresylate is an easily crystallizable solid, mp 76°, which solvolyzes at a convenient rate in the usual solvents at 25°. The rate constants measured by the precise conductance method[7,9] and isotope effects are given in Table I. It is apparent that the effects (1.225–1.228) are exactly as predicted for the mechanism involving rate-determining interconversion of ion pairs.[17,19] We, therefore, agree with the classification of this reaction as not involving solvent nucleophilic participation *in the rate-determining step*. It is further seen that in accord with this mechanism the isotope effect is not dependent on solvent polarity or nucleophilicity in the range 50E–97T. Within the experimental error of the less precise measurements the effect for isopropyl brosylate in TFA does not appear significantly different.[15] Independent evidence confirms that for this solvolysis k_2 is rate determining.[10] Thus three different sulfonate esters have now been observed to give the expected maximum α-D effect of $\sim$1.22. The fact that the α-D effect is at the maximum means that the initially formed ion pairs are undergoing internal return, *i.e.*, $k_{-1} > k_2$. Since the magnitude of this inequality is not known, care must be exercised in using the adamantyl compounds as reference substances to estimate unassisted *ionization* rates (k_1). By reference to the solvolysis rate of pinacolyl brosylate,[11] we estimate that the return to solvolysis rate ratio of the adamantyl tresylate tight ion pair (k_{-1}/k_2) is about 50. It is also apparent that α-CH_3/H ratios[26b] will depend on relative amounts of internal return.

We believe that carefully measured α-deuterium isotope effects provide the best probe known for determining *the degree of nucleophilic attachment to carbon in the rate-determining step* of a solvolytic substitution reaction. Isotopic substitution also has the unparalleled advantage of providing the *minimum* perturbation of the reaction under study. Thus, other criteria which have been applied such as the α-CH_3/H ratio,[26b] *m* values, $(k_{EtOH}/k_{HOAc})_y$,[26a] and salt effects always have a much more complex relationship to mechanism and depend on the comparison of mechanisms of two or more reactions. However, since solvolysis mechanisms are reasonably complicated it is apparent that any systematic attempt to understand the details must use the entire range of techniques which has been developed. This is especially important because of the synergistic effects of information from different sources such as relative rates, isotope effects, product ratios, and stereochemical results.

Table I. α-D Effects on Solvolysis of 2-Adamantyl 2,2,2-Trifluoroethylsulfonate, 25°

Solvent[a]	k_H, 10^{-5} sec^{-1}	$k_H/k_{\alpha\text{-D}}$
70T	29.795	1.225 ± 0.001
97T	17.05	1.228 ± 0.001
50E	8.172	1.225 ± 0.001

[a] 97T is 97% 2,2,2-trifluoroethanol–3% water, etc. 50E is 50 vol % ethanol–50 vol % water at 25°.

Acknowledgments. We thank Professor P. v. R. Schleyer for calling the interesting 2-adamantyl system to our attention before publication of his results[26a-e] and for the exchange of manuscripts on α-D effects in the solvolysis of those compounds prior to publication.

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(22) Some confusion in the use of the term "limiting" appears inevitable. The original definition[23] was that in this class there was no covalent attachment of solvent in the transition state. By this definition rate-determining formation of the (noncovalently solvated) ion pair would be "limiting" as would rate-determining conversion of one ion pair into another or rate-determining dissociation of an ion pair. Because some reactions which had previously been classified as limiting were shown to involve rate-determining ion-pair interconversion (k_2) we have used the term in this narrower sense.[7,9] It is apparent that advancing knowledge in this field now makes a further definition of terms desirable.

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(28) It is a direct conclusion from theory[19] that the characteristic *maximum* α-deuterium effect will not be influenced by structural changes remote from the reaction site and that the same value should obtain for all sulfonate leaving groups.

Pyrimidine Phototetramer[1]

Sir:

A photoreaction possibly involving the 1,6 head-to-head–tail-to-tail dimerization of a thymine deriva-

(1) This publication is identified as no. NYO-2798-57.

tive, 6,4′-[pyrimidin-2′-one]thymine[2-4] (I), has been discovered. It results in the formation of a large ring compound, a cyclohexadecine derivative,[4] II.

Irradiation of I in water with either 360- or 313-nm light resulted in a decrease of the maximum absorbancy at 316 nm and the appearance of a spectrum similar to that of thymine with λ_{max} at 265 nm (Figure 1).[3] The presence of an isosbestic point may suggest the formation of a single photoproduct or products with identical chromophores. When the irradiated solution was allowed to stand at room temperature, the absorbancy at 265 nm decreased slowly. This decrease became more pronounced with higher concentrations. Finally, it was found that this decrease results from the slow separation of the photoproduct into tiny crystals.

An aqueous solution of I [0.03 m*M*; 22 l.; OD_{316} 0.23; pH 5.8] was irradiated with 360-nm light [G.E. BLB (black light with integral filter)] in an irradiator.[5] [Similar results were obtained with 313-nm light (F40BL).] The absorbed dose rate was 8.5×10^{-5} einstein/l. min. The solution was irradiated for 16 min. After evaporation, the pale yellow residue was dissolved in 25 ml of 0.5 *N* NaOH. After acidification (pH 2), microcrystalline precipitate soon appeared. The precipitate was collected and redissolved in concentrated ammonia. As the ammonia was allowed to escape, colorless crystals gradually formed. The purified product (70 mg, 55%) was collected and washed with ethanol and ether. The quantum yield is, therefore, 0.012 mol/einstein. [At higher concentrations (0.1–0.2 m*M*), the yields decreased to 25% even though all the I had reacted. A water-soluble product forms having a uv spectrum similar to II.]

Compound II does not decompose at temperatures >300°. It is insoluble in water, trifluoroacetic acid, dimethyl sulfoxide, acetonitrile, and alcohol. In dilute alkalies (NaOH, NH_4OH) and strong acids (concentrated H_2SO_4, HSO_3F), II is soluble and stable. The data from the nmr spectrum at 60 MHz [$\delta_{TMS}^{HSO_3F}$ 2.67 (complex A_2B_2, 4 H, CH_2CH_2), 4.88 (d, 2 H, CH, J = 1.5 Hz), 5.85 (d, 2 H, C=CH, J = 1.5 Hz), 7.15 (s, 2 H, NH), 8.10 ppm (s, 2 H, NH)] and the uv spectrum [pH 1.5–7, λ_{max} 265 nm (ϵ_{max} 1.56×10^4); pH 11.5, λ_{max} 296 nm (ϵ_{max} 1.62×10^4)] comply with II.

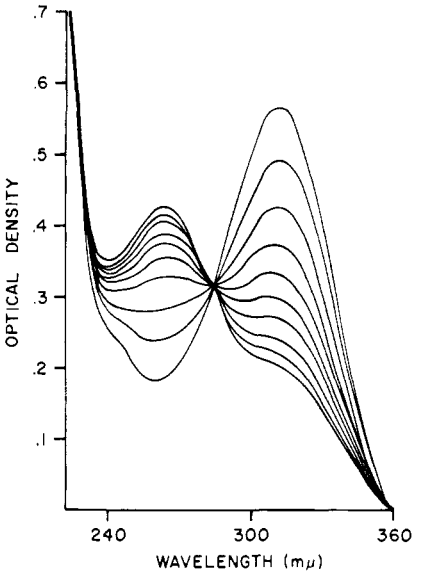

Figure 1. Uv spectra of 6,4′-[pyrimidin-2′-one]thymine in water irradiated (360 nm) at various time intervals (2 min).

In order to further substantiate its dimeric nature, 25 mg of II was subjected to repeated methylation with $(CH_3)_2SO_4$–NaOH. The $CHCl_3$ extract obtained from the reaction mixture gave a 29-mg yield of product [95% calculated as hexamethyl derivative of II]. The nmr data [δ_{TMS}^{DMSO} 2.50 (broad A_2B_2, 4 H, CH_2CH_2), 2.70 (s, 6 H, NCH_3), 3.21 (s, 6, H, NCH_3), 3.25 (s, 6 H, NCH_3), 4.13 (d, 2 H, CH, J = 1.5 Hz), 5.08 ppm (d, 2 H, C=CH, J = 1.5 Hz)] are consistent with the hexamethyl derivative of II. The assignments of the NCH_3 groups could not be made on the basis of these chemical shifts. However, these selections are plausible since the protons on N(8) and N(11) of II are much less acidic than the other nitrogen protons. Furthermore, methylation of dihydrouracil derivatives yields only monomethylated compounds with no alkylation on the amide nitrogen.[6] On the other hand, uracil derivatives give dimethylated compounds. On paper chromatography of methylated II with 2-propanol–ammonia–water (70:20:10, v/v), two bands with R_f 0.72 (86%) and 0.61 (14%) were observed. Both eluates showed λ_{max} at 268 nm and exhibited identical uv spectra at all pH (2–12), in contrast to the pH dependency of II. This observation suggests that both products are stereoisomers. The R_f 0.61 product was recrystallized from water after its aqueous solution was allowed to stand at 5° for 2 or 3 days. Its mass spectrum shows a parent peak at *m/e* 524 corresponding to hexamethylated II [$C_{18}H_{10}N_8O_6 \cdot 6CH_3$]. The major product formed large crystals after the solution was allowed to stand at room temperature for an extended period. The X-ray diffraction analysis of one of these crystals establishes the structure and the stereoconfiguration of II as trans-syn [9*S*,10*S*].[7] The minor product is thus very probably the cis-syn [9*S*,10*R*] isomer.

The first step is probably light induced and involves hydrogen transfer, as shown in Scheme I. It is hetero-

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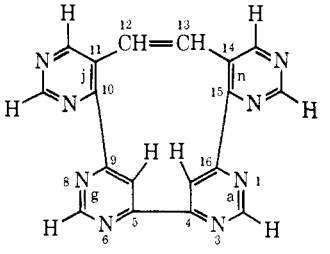
(4) The authors thank Dr. K. L. Loening, Director of Nomenclature, Chemical Abstract Services, for the naming of the compounds in this paper: I, 5-methyl[4,4′-bipyrimidine]-2,2′,6(1*H*,1′*H*,3*H*)-trione; Ia, 5-methylene[$\Delta^{4,4'(3H,1'H)}$-*bipyrimidine*]-2,2′,6(3*H*,3′*H*,5*H*)-trione; the parent ring system of compound II, 9,5:10,14-dimethenodipyrimido-[4,5-*j*:5′,4′-*n*][1,3,6,8]tetraazacyclohexadecine, as shown; II, R = H,



4,8,9,10,11,15,19,20-octahydro(parent ring system)-1,3,7,12,16,18-(2*H*,6*H*,13*H*,17*H*)-hexone; II, R = CH_3, 4,8,9,10,11,15,19,20-octahydro-2,4,6,13,15,17-hexamethyl(parent ring system)-1,3,7,12,16,18-(2*H*,6*H*,13*H*,17*H*)-hexone; IV, 5-(hydroxymethyl)uracil; V, 5-methylhydrouracil; VI, 5-methyl-5-[(1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl)methyl]hydrouracil; VII, 3-[(hexahydro-5-methyl-2,4-dioxo-5-pyrimidinyl)thio]alanine.

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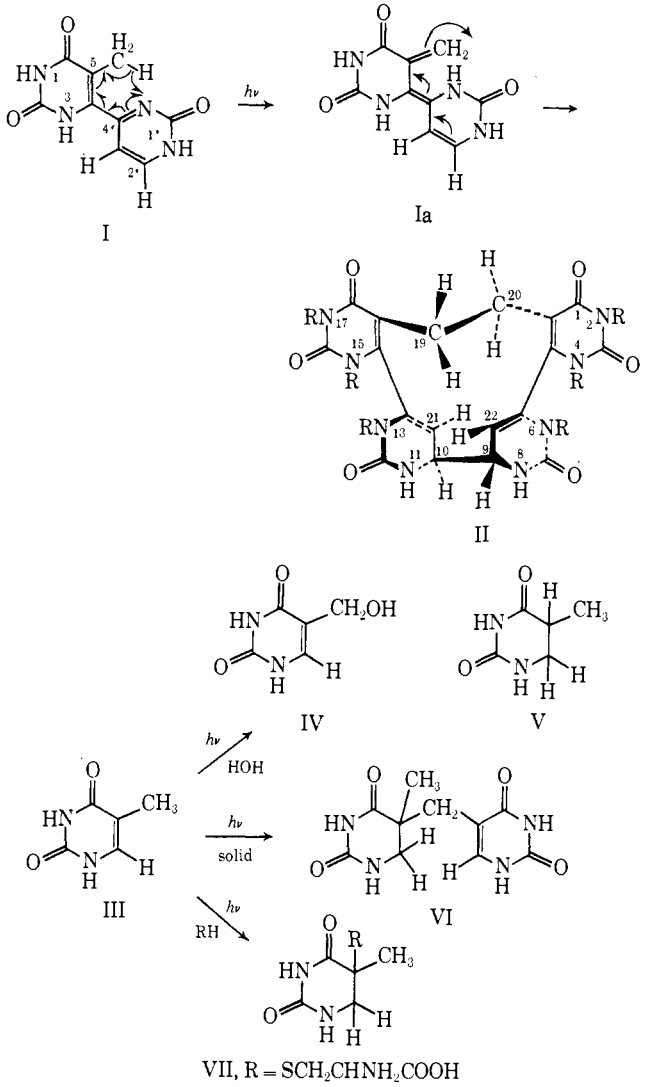
Scheme I



analogous to the well-known Norrish type II γ-hydrogen abstraction reactions of carbonyl compounds[8] and similar to the photochemical alloxazine–isoalloxazine transformation.[9] The resulting conjugated triene intermediate Ia should be a planar molecule. However, a molecular model shows that the exocyclic methylene group is forced out of the plane of the molecule and may be quite reactive. Thus, dimerization in a concerted manner ensues with another Ia approaching either from the same side to give a cis-syn dimer or from the opposite but stereochemically favored direction to yield a trans-syn isomer. Interestingly, the molecular model shows that the head-to-tail dimerization process is sterically unfavorable and explains why only dimers with syn or head-to-head configuration are obtained. While this mechanism seems to be the most likely choice, the detailed study is currently under way.

It should be noted that this hydrogen-transfer reaction may be related to the observation that irradiation (254 nm) of thymine III in aqueous solutions gives 5-hydroxymethyluracil (IV),[10] in DNA yields dihydrothymine (V),[11] and in solid state forms 5-thyminyldihydrothymine (VI).[12] In the presence of cysteine in aqueous solutions, irradiation of thymine results in the formation of 5-cysteinyldihydrothymine (VII). These reactions are of interest in the photo- and radiation chemistry of nucleic acids

Thus, the present finding indicates the occurrence of the hydrogen abstraction reaction in thymine derivatives. Also, it suggests that such a reaction could occur in DNA if the longer light wavelengths were absorbed by some chromophoric groups or by certain energy-transfer processes. Furthermore, reactions induced by thyminyl radicals may explain why 300–360-nm light causes inactivation in some biological systems.[13,14]

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Crystal and Molecular Structure of a Pyrimidine Phototetramer

Sir:

A product derived from an adduct of cytosine–thymine was separated from the acid hydrolysates of DNA irradiated with ultraviolet light *in vitro* and *in vivo*.[1] Its structure was characterized[2] as 6,4′-[pyrimidin-2′-one]thymine [$C_9H_8N_4O_3$] (I). Since I was obtained from the irradiation of DNA, its possible importance in the photobiology of nucleic acids should be investigated. However, only minute quantities of I can be isolated in these *in vivo* and *in vitro* experiments; thus, other approaches[3] must be developed in order to obtain sufficient amounts for further study. Consequently, it was found that the irradiation of a uracil–thymine mixture in frozen state can yield I in about 20 mg per run.[4] Upon irradiation of I in water with either 313- or 360-nm light, a novel photoreaction was discovered[5] involving 1,6-dimerization to form a large ring compound, II. Repeated methylation with methyl sulfate produced hexamethylated derivatives of two stereoisomers of II. The minor product (14%)

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