

PHOTOCHEMICAL SYNTHESIS OF THE FUSED TRICYCLIC COMPOUNDS

FROM BIS-6,6'-(1,3-DIALKYLURACILYL)SULFIDES¹

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Photocyclization is a useful procedure to prepare condensed cyclic compounds. Thus, syntheses of thiophenes fused with a carbocyclic ring, such as benzothiophenes and naphthothiophenes, from unsaturated organic sulfides have been studied extensively.^{2,3} Recently, Senda et al.⁴ reported photocyclization of phenylthiouracils into benzothienopyrimidines.

During the course of our work on heterocyclic compounds we became interested in the photocyclization of bis-6,6'-(1,3-dialkyluracilyl)sulfides (I)⁵ to obtain heterocycles with a new ring system. We found that photocyclization of I is not formulated by a simple mechanism but it involves rather complicated processes. In this report we describe the identification of photocyclization products from I, and also discuss plausible mechanisms for the reaction.

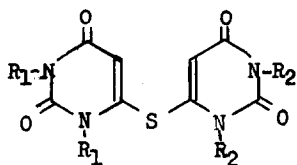
After irradiation⁶ of the sulfide Ia in tetrahydrofuran, three uv absorbing products, IIa (mp 300°, 18%), IVa (mp 266-269°, 8.2%) and VIa (mp 196°, 9%) were isolated from the mixture. Mass spectral (M^+) and microanalytical (C,H,N,S) data were consistent with the corresponding structures. The pmr spectrum of IIa showed only two singlets (see Table 1).

The formation of (1,4)dithiino(2,3-d;5,6-d')dipyrimidine structure IIa can readily be explained by dimerization of two uracil-6-thiol radicals followed by oxidation. The isomeric structure IIIa for this compound is eliminated because of the unusual low chemical shifts of the N-methyl signals. Studies with molecular models show that IIa takes a folded conformation and all the methyl groups come very close to carbonyls, whereas IIIa structure does not bring about this close proximity of methyl and carbonyl groups.

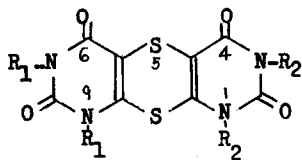
Table 1
Mass and pmr parameters of the photocyclization products
Chemical shifts (δ)^a

Compd.	(M ⁺)	NCH ₃ ^b				NCH ₂ CH ₃ ^c		NCH ₂ CH ₃ ^d			
		1	3	6	8	1	3	1	3	6	8
IIa	340	4.12	4.03	4.12	4.03			4.75			
IIb	396					1.28	1.36	4.75	4.10	4.75	4.10
IVa	308	3.92	3.42	3.60	3.40						
IVb	336	3.92	3.42			1.26	1.40			4.08	4.08
IVc	336			3.62	3.44	1.29	1.40	4.74	4.10		
V	364					1.25	1.40	4.08*	4.03**	4.03	4.08
VIa ^e	310	3.32	3.32	3.26	3.14						
VIb ^f	338	3.34	3.34			1.20	1.28			3.90	3.60

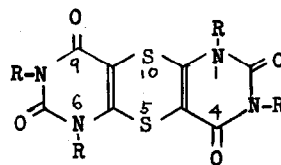
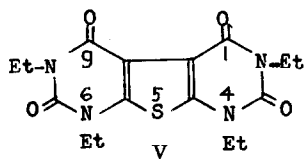
a) IIa was measured in DMSO-d₆, all others were determined in CDCl₃ b) singlet
c) triplet d) quartet e) two doublets at $\delta = 4.40$ and 5.96 ($J = 8.0$ Hz) f) two doublets at $\delta = 4.32$ and 5.96 ($J = 8.0$ Hz) * Actual position N-2. ** N-4.



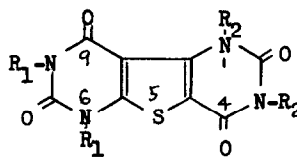
I a $R_1 = R_2 = \text{Me}$
b $R_1 = R_2 = \text{Et}$
c $R_1 = \text{Me}, R_2 = \text{Et}$



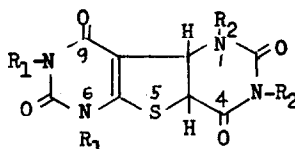
III a $R_1 = R_2 = \text{Me}$



II a $R = \text{Me}$
b $R = \text{Et}$

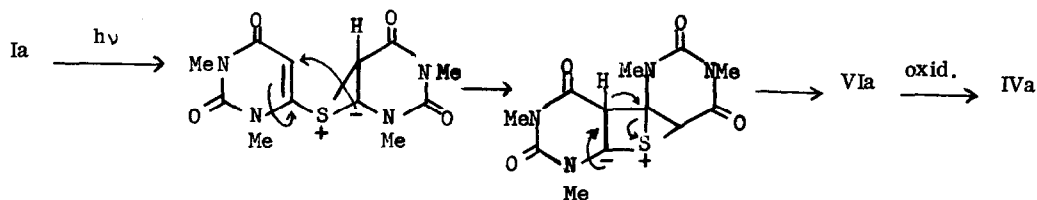


IV a $R_1 = R_2 = \text{Me}$
b $R_1 = \text{Et}, R_2 = \text{Me}$
c $R_1 = \text{Me}, R_2 = \text{Et}$



VI a $R_1 = R_2 = \text{Me}$
b $R_1 = \text{Et}, R_2 = \text{Me}$

The pmr spectrum of the second product showed the presence of four non-equivalent N-methyl groups in the molecule, thus establishing IV structure for this compound. The formation of dipyrimidino(2,3-d;4,5-d')thiophene system (IVa) can be formulated as an electrocyclic reaction involving an unusual rearrangement as shown below.



A similar mechanism was first proposed by Groen *et al.*² for the rearrangement of 1-phenyl-1-phenylthioethene into 3-phenylbenzo(b)thiophene by photocyclization. Schultz and DeTar³ later invoked this mechanism to explain the conversion of 1-(2-naphthylthio)-1-phenyl-1-propene into 2-methyl-3-phenylnaphtho(2,1-b)thiophene.

The third product of the photolysis of Ia showed a pair of geminal proton doublets in addition to singlets for the four N-methyl groups in the pmr spectrum. The structure of this compound is assigned to VIa which is an intermediate in the reaction Ia \rightarrow IVa. It should be noted that irradiation of IIA did not give IVa but resulted in a total recovery of the starting material. Thus, the intermediacy of IIA in the formation of IVa is ruled out.

Photocyclization of bis-6,6'-(1,3-diethyluracilyl)sulfide (Ib) under similar conditions, however, gave only two products, 1,3,6,8-tetraethyl(1,4)dithiino(2,3-d;5,6-d')dipyrimidin-2,4,7,9(1H,3H,6H,8H)tetraone, IIB (mp 160-162°, 11%) and the normal cyclization products, 2,4,6,8-tetraethyldipyrimidino(2,3-d;5,4-d')thiopen-1,3,7,9(2H,4H,6H,8H)tetraone, V (mp 204-206°, 13%). Only signals for two instead of the four N-ethyl appeared in the pmr spectrum of V. No rearrangement product such as IV or VI type was obtained.

In order to study the effects of N-substituents on photocyclization, unsymmetrical 6-(1,3-dimethyluracilyl)-6'-(1',3'-diethyluracilyl)sulfide (Ic) was synthesized⁵ and photolyzed. The major products IVb (mp 204-205°, 12%) and VIb (mp 170-173°, 6.5%) together with traces of IVa and IVc (mp 209-211°) were obtained. No dithiine of type II or no normal photocyclization product of type V was detected in the mixture. The IVb structure was

proved by the unusual low field shift of N-1 methyl signal in pmr spectrum. This paramagnetic shift is caused by the close proximity of N-1 methyl and C-9 carbonyl groups. Similarly, the methylene quartet of N-1 ethyl in IVc is observed at very low field (Table 1). The structure of dihydro compound is assigned to VIb which is a precursor of IVb. Compound VIb appeared to be oxidized slowly to IVb (mp 205-206°) by atmospheric oxygen on standing. Compound IVa obtained from this reaction probably arose from Ia which was formed by recombination of dimethyluracil-6-thiol radical and dimethyluracil radical.

It may be concluded from the above results that N-methyl substitution of I favors the rearrangement during photocyclization whereas the N-ethyl derivative of I gives the normal photosynthesis product V.

References

- 1 Presented in part at 97th Annual meeting of the Pharmaceutical Society of Japan, Tokyo, April, 5-7, 1977.
- 2 S. H. Groen, R. M. Kelloggs, J. Buter and H. Wynberg, *J. Org. Chem.*, **33**, 2218 (1968).
- 3 A. G. Schultz and M. B. DeTar, *J. Am. Chem. Soc.*, **96**, 296 (1974); **98**, 3564 (1976).
- 4 S. Senda, K. Hirota and M. Takahashi, *J. C. S. Perkin I*, 503(1975).
- 5 Compounds Ia and Ib were synthesized by coupling of 1,3-dialkyluracil-6-sodium mercaptide with 6-chloro-1,3-dialkyluracil, Ia, mp 248°, 72%; Ib, mp 125°, 12%. Compound Ic was prepared by condensation of 6-chloro-1,3-diethyluracil with 1,3-dimethyluracil-6-sodium mercaptide, mp 153-154°, 25%. Satisfactory microanalytical and pmr data were obtained.
- 6 Irradiations were carried out in a flask fitted with a 400w high pressure mercury lamp covered with a quartz filter for 9-15 hours under nitrogen.
- 7 Satisfactory elemental analyses compatible with the structural assignments were obtained for all the compounds with melting point described herein. Melting points are uncorrected.