$CHCH_2NH$-*n*-Bu, 4538-09-4; $CH_2$=$CHCH_2NHPh$, 589-09-3; MeI, 74-88-4; PhI, 591-50-4; PhCH=CHBr, 103-64-0; MeCOBr, 506-96-7; PhCOBr, 618-32-6; PhCOCl, 98-88-4; EtOCOCl, 541-41-3; $MeCONEt_2$, 685-91-6; $PhCONEt_2$, 1696-17-9; PhCH=$CHCONEt_2$, 3680-04-4; $MeCOCONEt_2$, 22381-21-1; $PhCOCONEt_2$, 34906-86-0; $EtOCOCONEt_2$, 5411-58-5; CO, 630-08-0; $LiNEt_2$, 816-43-3; $CH_2$=$CHCH_2Br$, 106-95-6.

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## Photooxidation of Dimethylthymine: Contrasting Regio- and Stereospecific Reactions of the Initial Photoproduct with Nucleophiles

*Summary:* Postirradiation treatment of photooxidized 1,3-dimethylthymine with phenol resulted in the formation of the unexpected carbon–carbon coupling products, *cis*-5-hydroxy-6-[*p*- or *o*-hydroxyphenyl]-1,3-dimethyl-5,6-dihydrothymine (**6a** and **6b**), rather than the anticipated 6-phenoxy adduct analogous to the products observed with other oxygen and sulfur nucleophiles, thus indicating two different mechanistic pathways for ring opening of the initial epoxide which may be of significance in chemical reactions of biological importance.

*Sir:* Recently, we reported the preliminary study of photooxidation of pyrimidines (**1a,b**)[1] using $\alpha$-diketones (**2a,b**) as sensitizers.[2] The results suggest the formation of highly reactive pyrimidine 5,6-epoxides (**3**) as intermediates[1] (Scheme I). Subsequently, studies of the reactions of *trans*-5-bromo-6-hydroxy-5,6-dihydrothymines with nucleophiles in the presence of bases provide more definitive evidence for the formation of **3**.[3] **3** is attacked readily by nucleophiles to give adducts which in one case were shown to be primarily of cis configuration.[1] In this communication we establish conclusively the structures and configurations of three adducts which are indicative of *two different mechanistic pathways depending on the nature of the nucleophile.* Postirradiation treatment of photooxidized[4] dimethylthymine (**1a**) with water, acetic acid, or thiophenol as nucleophiles gave exclusively the cis adducts **5a–c** in the yields indicated, with no evidence for the presence of a trans isomer in any case.[5] Glycol **5a** and its trans isomer have been independently synthesized,[6] and **5b** was shown to be cis by its facile hydrolysis to **5a** on a silica gel plate. Since stereochemistry of 5,6-dihydropyrimidines cannot be assigned on the basis of $^1H$ NMR chemical shifts alone, even when both isomers are available, a single-crystal X-ray diffraction analysis of **5c** was performed (see below).

In contrast, postirradiation treatment of photooxidized **1a** with phenol gave (80% yield) a 3:2 mixture of two isomeric adducts which we suggested initially were *cis*- and *trans*-5-hydroxy-6-phenoxy-1,3-dimethyl-5,6-dihydrothymines. However, reexamination of the 100-MHz $^1H$-NMR spectrum of the major isomer (mp 204 °C) showed that, in addition to the previously described[1] broad singlet at $\delta$ 8.18 originally attributed to C-5 **OH**, a second broad singlet at $\delta$ 3.92 can be seen, and the integral of the multiplet at $\delta$ 6.80 corresponded more closely to 4 H than to 5 H. A single-crystal X-ray diffraction analysis (see below) confirmed that the major isomer was the unexpected carbon–carbon coupling product **6a** and established its configuration as cis. The minor isomer, obtained initially as a viscous oil, crystallized slowly and was purified by recrystallization from benzene, mp 175 °C. Its NMR spectrum, unlike that of the major isomer, did not reveal a clue as to its identity. Singlets for the C-5 $CH_3$, the two N-$CH_3$ groups, and C-6 H at $\delta$ 1.71, 3.06, 3.27, and 4.71, respectively, and a multiplet at $\delta$ 6.63–7.20 integrating for 4–5 H were the only signals observed. However, its identity as the *o*-hydroxy adduct **6b**, also of cis configuration, was established by X-ray diffraction analysis. No other isomeric adduct was detected.

Table I

| compound | **5c** | **6a** | **6b** |
|---|---|---|---|
| crystal class | monoclinic | monoclinic | monoclinic |
| space group | $P2_1/n$ | $P2_1/c$ | $P2_1/c$ |
| *a*, Å | 11.100 (3) | 13.056 (4) | 8.363 (3) |
| *b*, Å | 11.326 (3) | 8.317 (3) | 12.434 (4) |
| *c*, Å | 11.026 (3) | 13.478 (6) | 12.406 (5) |
| $\beta$, degrees | 96.2 (1) | 117.4 (1) | 103.6 (1) |
| *Z* | 4 | 4 | 4 |
| radiation | Cu K$\alpha$ | Cu K$\alpha$ | Mo K$\alpha$ |

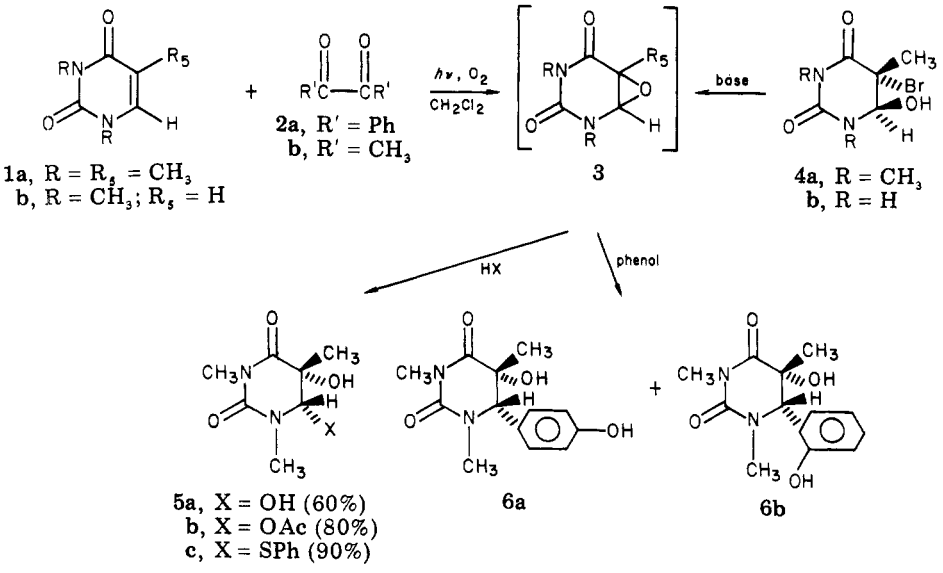
Pertinent physical constants, derived from the X-ray work, for the crystals of **5c**, **6a**, and **6b** are given in Table I. All three structures were solved by the symbolic addition procedure for centrosymmetric crystals.[7] The results are displayed in the stereodiagrams[8] in Figure 1. In all three compounds the heterocyclic ring has five coplanar atoms (±0.1 Å) and the sixth atom C-6 in **5c** and **6b** and C-5 in **6a** lies approximately 0.6 Å from the plane. In **5c** the sulfur atom forms a bridge between the two rings which are almost parallel to one another. In **6a** and **6b** the two rings are essentially perpendicular to one another.

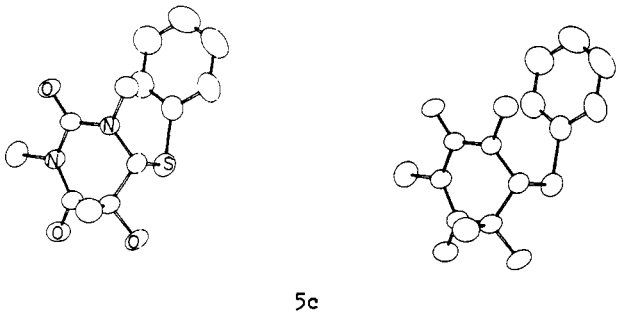
In the initial work prior to the structural determinations of the phenol adducts it was apparent that, if a pyrimidine 5,6-epoxide was indeed an intermediate photoproduct, it did not undergo $S_N2$ attack by nucleophiles to give trans products. To account for the predominance or exclusive formation of cis products, we had envisioned this as one of the electronegatively substituted systems where gauche interactions[9] are important and the epoxide intermediate is sufficiently stabilized by zwitterionic contributions to allow nucleophilic attack from an energetically favored direction giving cis adducts.[1] The cis carbon–carbon bonded phenol adducts may be regarded as products of electrophilic attack at the ortho and para positions of phenol, but the possibility of a radical coupling mechanism[10] cannot be excluded.

(1) H.-S. Ryang and S. Y. Wang, *J. Am. Chem. Soc.*, **100**, 1302 (1978).
(2) N. Shimizu and P. D. Bartlett, *J. Am. Chem. Soc.*, **98**, 4193 (1976).
(3) H.-S. Ryang and S. Y. Wang, *J. Org. Chem.*, **44**, 1191 (1979).
(4) Experimental conditions for the photooxidations are given in ref 1, footnote 5.
(5) Reaction products were separated by preparative TLC on silica gel with 3:2 $CHCl_3/CH_3CN$ as eluent.
(6) L. R. Subbaraman, J. Subbaraman, and E. J. Behrman, *J. Org. Chem.*, **38**, 1499 (1973).
(7) J. Karle and I. L. Karle, *Acta Crystallogr.*, **21**, 849 (1966).
(8) The stereodrawings were drawn from the experimental results using program ORTEP: C. K. Johnson, Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, Tenn.
(9) E. L. Eliel, *Acc. Chem. Res.*, **3**, 1 (1970); R. J. Abraham, H. D. Banks, E. L. Eliel, O. Hofer, and M. K. Kaloustian, *J. Am. Chem. Soc.*, **94**, 1913 (1972).
(10) A. I. Scott, *Q. Rev., Chem. Soc.*, **19**, 1 (1965); E. R. Altwicker, *Chem. Rev.*, **67**, 475 (1967).

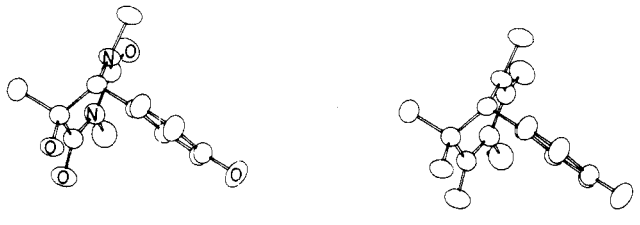
0022-3263/79/1944-3736$01.00/0 

Scheme I

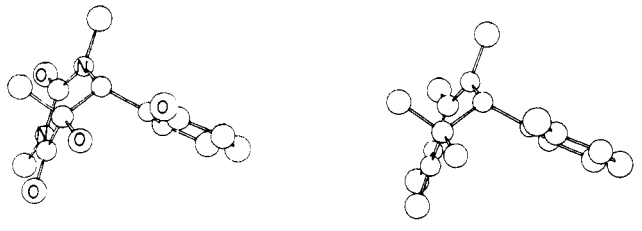


5c



6a



6b

**Figure 1.** Stereodiagrams of **5c**, **6a**, and **6b**.

This unique behavior of phenol and the importance of photochemical formation of nucleic acid–protein cross linkages in biological systems[11] prompted us to report these findings which should be of wide interest. Currently, the scope and stereochemistry of this novel photoreaction with other nucleophiles and amino acid derivatives are under investigation.

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**Registry No.** **1a**, 4401-71-2; **1b**, 874-14-6; **2a**, 134-81-6; **5a**, 38645-23-7; **5b**, 71516-72-8; **5c**, 71516-73-9; **6a**, 71516-74-0; **6b**, 71516-75-1; thiophenol, 108-98-5; phenol, 108-95-2.

**Supplementary Material Available:** Experimental Section describing the preparation of **5c**, **6a**, and **6b** (1 page). Ordering information is given on any current masthead page.

(11) K. C. Smith in "Photochemistry and Photobiology of Nucleic Acids. Biology", Vol. 2, S. Y. Wang, Ed., Academic Press, New York, 1976, Chapter 5, p 187; M. P. Gordon, C. W. Huang, and J. Hurter, *ibid.*, Chapter 7, p 270; K. C. Smith, in "Aging, Carcinogenesis, and Radiation Biology", K. C. Smith, Ed., Plenum Press, New York, 1976, p 67.

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## A New Reducing System: Calcium Metal in Amines. Effect of Hexamethylphosphoramide on Calcium Reductions

*Summary:* A new reducing system is described wherein calcium metal in methylamine–ethylenediamine reduces simple aromatics cleanly to monoolefins. It is also disclosed that reduction rate and product selectivity are greatly enhanced in the calcium hexammine–ether system by the addition of small amounts of HMPA.

*Sir:* We wish to report that calcium metal dissolved in a mixture of methylamine and ethylenediamine provides an excellent medium for the reduction of various aromatics to monoolefins. This is the first report of the successful

 