Table II. Comparative Inhibition of L1210 Leukemia *in Vivo* by 4-Peroxycyclophosphamide and by Cyclophosphamide

Compound	Innoculum of leukemic cells	Dose (mg/kg)	Increase in life span (%) (in dying animals)	30-day survivors
4-Peroxycyclo-phosphamide	10^6 (IP)	250	175	3/10
		200	100	2/10
Cyclophosphamide		300	93	0/10
		200	87	1/10
		133	50	0/10
4-Peroxycyclo-phosphamide	10^7 (IV)	250	200	0/10
		200	175	0/10
Cyclophosphamide		312	237	0/10
		156	162	0/10

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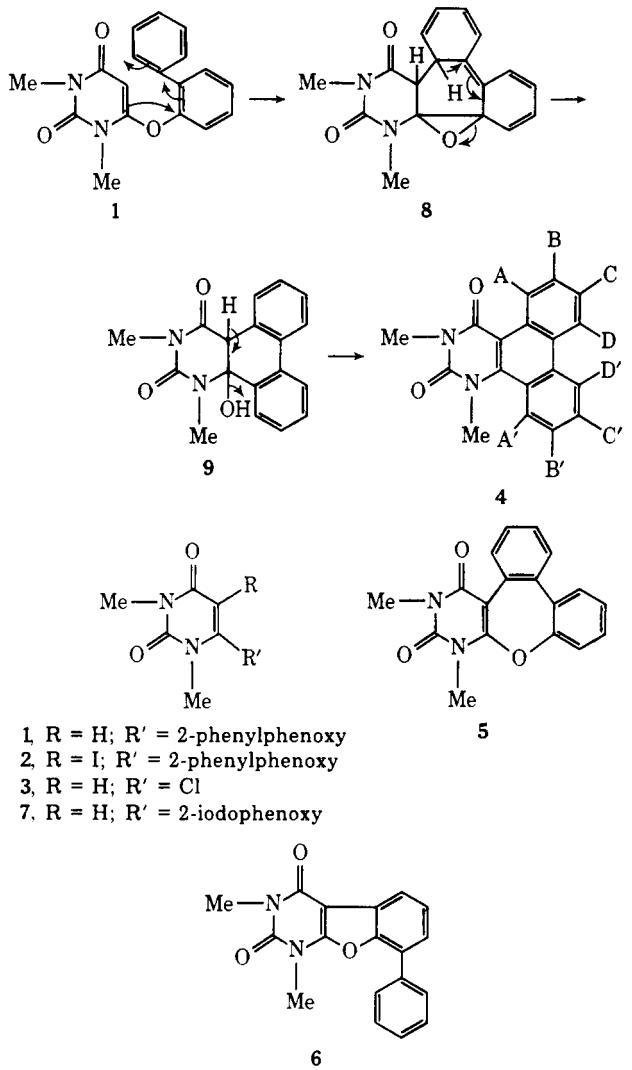
Photocyclodehydration of 6-*o*-Biphenyloxy-1,3-dimethyluracil

Sir:

Photochemical cyclodehydrogenation of stilbenes[1] and related compounds[2] and photocyclodehydrohalogenation of their substituted ortho iodo derivatives[3] has been reported to produce mostly a six-membered[1–3] and rarely a five-membered ring.[4]

In general,[5] photocyclodehydrogenation occurs through a cyclic system,[1] while photocyclodehydrohalogenation occurs through an aromatic radical intermediate.[4]

In an effort to further extend our understanding of the mechanism of photocyclization reactions, we have investigated the photolytic behavior of 6-*o*-biphenyloxy-1,3-dimethyluracil (**1**) and 5-iodo-6-*o*-biphenyloxy-1,3-dimethyluracil (**2**). These two compounds are of particular interest in two ways. First, the mode of their cyclization process may be different thus leading to distinct products. In addition, since they exhibit two alternative positions for cyclization, that is ring closure between C_5 of the pyrimidine nuclei and C_6' or C_8' of the biphenyloxy group thus leading to a five- or seven-membered ring formation, respectively, competition between the two may exist.



The synthesis of **1**[6] (mp 154–155°; nmr (CCl_4) δ 3.12 (s, NMe, 3 H), 3.28 (s, NMe, 3H), 4.52 (s, C_5H, 1 H), 7.38 (m, aromatic H, 9 H); mass spectrum *m/e* 308 (M^+)) was accomplished by replacement of the chlorine of 6-chloro-1,3-dimethyluracil[7] (**3**) with an *o*-biphenyloxy group using a solution of sodium *o*-biphenyloxide. Its iodo derivative (**2**)[6] (mp 172–173°; nmr ($CDCl_3$) δ 3.24 (s, NMe, 3 H), 3.42 (s, NMe, 3 H), 7.18–7.62 (m, aromatic H, 9 H); mass spectrum *m/e* 434 (M^+)) was obtained by acetomercuration followed by iodination[7] of **1**.

Irradiation of **1** in benzene in 16 hr near room temperature in a cylindrical quartz cell or quartz tube utilizing the light from a Hanovia 100-W mercury lamp led to the tetracyclic **4**[6,8,9] (mp162–163°; nmr ($CDCl_3$) δ 3.52 (s, NMe, 3 H), 3.75 (s, NMe, 3 H), 7.94 (m, 4 H, $H_C + H_B + H_C' + H_B'$), 8.13 (dd, $J = 8.1, J = 1.5$ Hz, H_A'), 8.40–8.73 (m, 2 H, $H_D + H_D'$), 9.78 (dd, $J = 8.2$, $J = 2.5$ Hz, 1 H, H_A); mass spectrum *m/e* 290 (M^+)) while

(1) A. Bomber, K. A. Muszkat, and E. Fischer, *Isr. J. Chem.*, **10**, 765 (1972).
(2) C. E. Loader and C. J. Timmons, *J. Chem. Soc.*, 1678 (1967).
(3) J. Blum, F. Grauer, and E. D. Bergmann, *Tetrahedron*, **25**, 3501 (1969).
(4) W. A. Henderson, R. Lopresti, and A. Zweig, *J. Amer. Chem. Soc.*, **91**, 6049 (1969); W. A. Henderson and A. Zweig, *Tetrahedron Lett.*, 625 (1969).
(5) Contrary to these, suggested mechanisms have also been reported: R. Srinivasan and J. N. C. Hsu, *J. Amer. Chem. Soc.*, **93**, 2816 (1971); G. DeLuea, G. Martelli, P. Spagnolo, and M. Tiecco, *J. Chem. Soc.*, 2504 (1970).
(6) Elemental, nmr, uv, and mass spectra analysis are in complete agreement with the proposed structures.
(7) W. Pfleiderer and H. Deiss, *Isr. J. Chem.*, 603 (1968).
(8) The same substance was obtained from the irradiation of 5,6-diiodo-1,3-dimethyluracil in benzene, which will be reported in the near future.
(9) There is a certain similarity between the nmr of **4** and phenanthrene: F. A. Bovey, "Nuclear Magnetic Resonance Spectroscopy," Academic Press, New York, N. Y., 1969, p 68.

photolysis of **2** in 5 hr led to 21% of **5**[6] (mp 257–259°; nmr ($CDCl_3$) δ 3.36 (s, NMe, 3 H), 3.67 (s, NMe, 3 H), 7.18–7.96 (m, aromatic H, 8 H); mass spectrum *m/e* 306 (M^+)) and 3% of **6** (mp 257–259°; nmr ($CDCl_3$) δ 3.40 (s, 2NMe), 7.22 (s, aromatic H), 7.15–7.92 (m, aromatic H); mass spectrum *m/e* 306 (M^+)).

In the case of photolysis of **2**, the results are consistent with a mechanism where the initial photochemical step is a homolytic cleavage of C-1 to give an aromatic radical. The radical may then undergo cyclization in the position 6′ and 8′ of the biphenoxy group to give the observed **6** and **5**, respectively.

To further investigate the mechanism for the formation of the tetracyclic **4**, 6-(2-iodophenoxy)-1,3-dimethyluracil (**7**) (mp 179–181°; nmr ($CDCl_3$) δ 3.32 (s, NMe, 3 H), 3.59 (s, NMe, 3 H), 4.65 (s, C_5H, 1 H), 7.05–8.15 (m, aromatic H, 4 H); mass spectrum *m/e* 358 (M^+)) was synthesized by the same procedure as for **1**, using sodium 2-iodophenoxide as replacing agent and irradiated under similar conditions for 3 hr to give **1**, **4**, and **7**. On continuation for another 8 hr, substance **1** disappeared in favor of **4**.

To show that **4** is not obtained from the reaction of 1,3-dimethyl-6-uracil radical, a possible intermediate due to cleavage of the C–O bond in **1** and **7** and the solvent benzene, the irradiation of **1** and **7** was carried out in hexadeuterated benzene. The base peak in the mass spectrum of the isolated **4** from **1** was at *m/e* 290 (M^+) and from **7** at *m/e* 294 (M^+) and the base peak of the isolated **1** from **7** was at *m/e* 313 (M^+), indicating the inclusion of the solvent only in the latter case. It is thus feasible to consider the intermediates **8** and **9** as the precursor to **4** which is a rather unique process.

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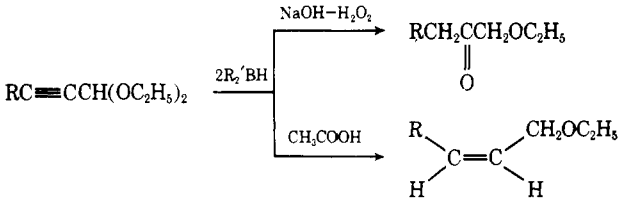
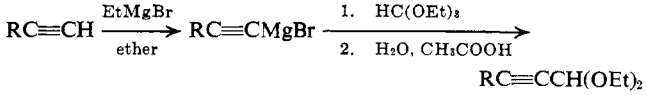
Novel Syntheses of α-Keto Ethers and *cis*-Allylic Ethers *via* the Hydroboration of Acetylenic Acetals[1]

Sir:

We wish to report operationally simple, high yield, stereoselective procedures for preparing α-keto ethers or *cis*-allylic ethers *via* the hydroboration of acetylenic acetals with dialkylboranes. This is followed by treatment of the intermediate organoborane with alkaline hydrogen peroxide or with acetic acid, respectively.



The acetylenic acetals themselves are readily obtained from terminal alkynes in greater than 80% yields by the following procedure.[2]



Hydroboration of 1,1-diethoxy-2-heptyne with 1 equiv of disiamylborane [bis(3-methyl-2-butyl)borane] in tetrahydrofuran solvent, followed by oxidation of the resultant organoborane with alkaline hydrogen peroxide, yielded 40% of a mixture of 1-ethoxy-2-heptanone and 1,1-diethoxy-3-heptanone along with 50% of the unreacted starting material. Complete utilization of the acetylenic acetal was achieved by employing 2 equiv of the hydroborating agent. Oxidation of the intermediate organoborane in this case afforded a 76 to 24% mixture of keto ether and keto acetal in a 90% yield, as evidenced by glpc analysis.

Although mixtures of keto ether and keto acetal were obtained when the alkyl group of the acetylenic acetal was primary, substitution by a secondary or tertiary alkyl group resulted in formation of essentially pure α-keto ethers. For example, sequential treatment of 1,1-diethoxy-4,4-dimethyl-2-pentyne with 2 equiv of disiamylborane, then with alkaline hydrogen peroxide, produced an 85% isolated yield of 1-ethoxy-4,4-dimethyl-2-pentanone containing less than 1% of the corresponding keto acetal. Furthermore, treatment of the hydroboration product with glacial acetic acid afforded 1-ethoxy-*cis*-4,4-dimethyl-2-pentene in a 79% yield.[3]

Some representative conversions of various acetylenic acetals into the corresponding keto ethers and *cis*-allylic ethers are shown in Table I.

Table I. Isolated Yields of α-Keto Ethers and *cis*-Allylic Ether Derived from Acetylenic Acetals

$RC{\equiv}CCH(OC_2H_5)_2$	Yield of α-keto ether, %[a]	Yield of *cis*-allylic ether, %[a]
R = *n*-C_4H_9–	61[b]	65
i-C_3H_7–	85	83
t-C_4H_9–	85	79[c]
	80	81
	81	81
	81	86

[a] The spectral and microanalytical data for all new compounds reported are consistent with the structures proposed. [b] No difficulties were encountered in distilling the α-keto ether from the by-product, 1,1-diethoxy-3-heptanone. [c] Glpc analysis revealed a 95 to 5 mixture of the cis and trans ethers.

The following experimental procedures are representative. To a solution of disiamylborane[4] (105 mmol) in THF (150 ml) was added at 0–5° a solution of 1,1-diethoxy-3-cyclopentyl-2-propyne (50 mmol) in THF (15 ml), precooled to −25°. The reaction mixture was stirred at 0° for 30 min, then at 25° for 1 hr. The resultant organoborane was oxidized by the addition of 30 ml of 6 *N* sodium hydroxide and 30 ml of 30%

(1) This research was supported by the National Science Foundation through Grant No. GP-26360.

(2) A. L. Kranzfelder and R. R. Voget, *J. Amer. Chem. Soc.*, **60**, 1714 (1938).

(3) In the case of 1,1-diethoxy-2-heptyne, protonolysis of the hydroboration product should afford besides the allylic ether, 1,1-diethoxy-*cis*-3-heptene. However, isolation of this compound has thus far eluded us.

(4) G. Zweifel, G. M. Clark and N. L. Polston, *J. Amer. Chem. Soc.*, **93**, 3395 (1971).