of bromine dropwise. This bromination solution was added to a mixture of 340 ml of anisole and 113 g (0.84 mol) of $AlCl_3$ in a 1-l. three-necked flask equipped with mechanical stirrer. The mixture was heated to 80–90° for 1 hr with stirring and then was stirred at room temperature for 2 hr. The mixture was poured into 500 g of ice and acidified with 75 ml of concentrated HCl. The organic layer was separated and the aqueous layer was extracted with 1 l. of ether. The combined organic layers were washed with water, dilute NaOH, and water. The dried solution was concentrated under reduced pressure. The residue was distilled to give 80 g of product bp 180–190° (0.08 mm). Recrystallization of the product from methanol twice gave 54 g of colorless crystals: mp 93–94.5°; ir 1602 cm^{-1} (C=C conjugated); uv λ_{max} (isooctane) 285 mμ (ϵ 14,840) and 247 (21,653); nmr δ 7.13 (s, 5, aromatic), 7.3 (q, 4, aromatic, J_{AB} = 9 Hz), 6.68 (q, 4, aromatic, J_{AB} = 9 Hz), 3.8 (s, 3, OCH_3), 3.66 (s, 3, OCH_3), and 2.13 (s, 3, CH_3). A mixture melting point with the product obtained from method A showed no depression.

Ozonolysis of 1,1-Bis(*p*-methoxyphenyl)-2-phenylpropene (4).—A solution of 3 g of the olefin 4 in 200 ml of ethyl acetate was cooled in a Dry Ice–acetone bath. A stream of ozone was passed into the solution. After about 20 min, the solution became light blue. Ozone was passed into the solution for another 30 min. The ozone generator was switched off and oxygen was passed through the solution for 20 min. The flask was removed from the Dry Ice–acetone bath and dry nitrogen was passed through the solution for 20 min. The solvent was removed under reduced pressure to give a yellow mixture of solid and oil. The residue was stirred in 25 ml of acetic acid and 1 g of Zn dust for 1 hr at room temperature. The mixture was diluted with 300 ml of ether and was filtered through Celite. The clear filtrate was washed with 2 × 200 ml of water and dilute $NaHCO_3$ solution until neutral. The ether solution was dried and concentrated to give a semisolid. Recrystallization from alcohol gave 1.5 g of product, mp 141–143°. Recrystallization again from hexane gave tiny needles, mp 142–143°. Dimethoxybenzophenone from Aldrich, recrystallized twice, melted at 142–144°. A mixture melting point showed no depression. Both materials showed the same spot on tlc (20% ethyl acetate in benzene). The ir, uv, and nmr spectra of both materials were also identical.

Acetophenone was detected by tlc in the alcoholic mother liquor, but no attempt was made to isolate it.

Registry No.—**1**, 23022-83-5; **4**, 33835-17-5; ethyl 2-phenylpropionate, 2510-99-8.

Acknowledgment.—This research was supported by a grant from the Population Council, Contract No. AID/csd-2491.

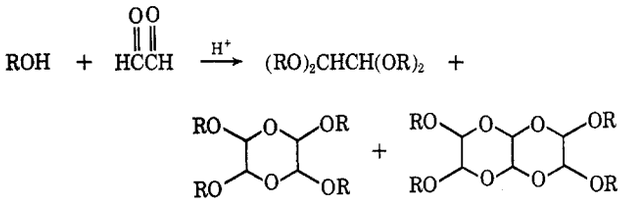
Glyoxal Derivatives. IV. 2-Dimethoxymethyl-4,5-dimethoxy-1,3-dioxolane and 2,2′-Bis(4,5-dimethoxy-1,3-dioxolane)

J. M. KLIEGMAN,*[1a] E. B. WHIPPLE,[1b] M. RUTA,[1b] AND R. K. BARNES[1a]

Research and Development Department, Chemicals and Plastics Division, Union Carbide Corporation, South Charleston, West Virginia 25303, and Tarrytown Technical Center, Tarrytown, New York 10591

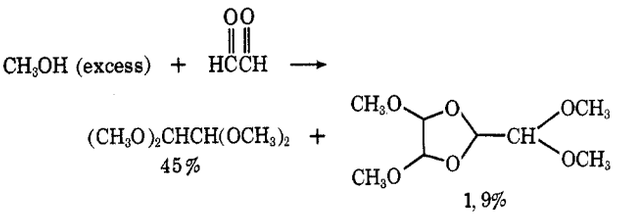
Received August 30, 1971

The reaction of aqueous glyoxal with alcohols to give bisacetals is well known and has been the subject of two basic patents.[2] General descriptions of the preparation of tetraalkoxyethanes, tetraalkoxydioxanes, and tetraalkoxynaphthodioxanes from aqueous glyoxal and

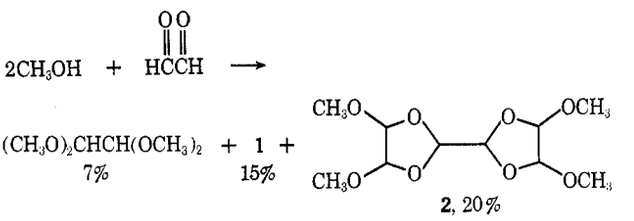


butanol or isopropyl alcohol have also been published.[3] The reaction of glyoxal with methyl alcohol, or glyoxal sulfate with methyl alcohol in the presence of calcium chloride, has also been reported.[4,5] In those cases the only product isolated was 1,1,2,2-tetrakis(methoxy)-ethane. In this paper we report the isolation and identification of two totally new acetal derivatives of glyoxal based upon the dimeric and trimeric forms of glyoxal.

We have found that 80% glyoxal reacts with methyl alcohol under acid conditions to give, as previously reported, 1,1,2,2-tetrakis(methoxy)ethane and a new compound, 2-dimethoxymethyl-4,5-dimethoxy-1,3-dioxolane (**1**), in 45 and 9% yields, respectively. If the



reaction is run with only 2 mol of methyl alcohol/mol of glyoxal the higher molecular weight dimer and a trimer, **2**, predominate. In both of these reactions



substantial amounts of intractable residues were produced.

The structures of compounds **1** and **2** were deduced from their molecular weights, carbon and hydrogen analyses, and proton magnetic resonance spectra. In the case of compound **2**, no reasonable alternative to the assigned structure exists, apart from diastereoisomerism. The final choice between two possible structures for compound **1** is based upon interpolation between the rigorously assigned structure of glyoxal dimer[6] and compound **2**.

The elemental analysis and molecular weight of compound **2** are supportive for a trimer of glyoxal with four methoxyl groups. The pmr spectrum in deuteriochloroform at 60 MHz shows one strong line at 3.41 ppm (downfield from tetramethylsilane) representing the four methoxyl groups and three equally intense

(1) (a) Tarrytown; (b) South Charleston.

(2) (a) C. B. Purves, U. S. Patent 2,194,405 (March 19, 1940); (b) L. G. MacDowell and R. W. McNamee, British Patent 559,362 (Feb 16, 1944).

(3) "General Chemistry of Glyoxal," Union Carbide Product Booklet, 1965, p F-41296.

(4) H. O. L. Fisher and C. Taube, *Chem. Ber.*, **59B**, 851 (1926).

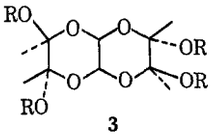
(5) D. H. Graangard and C. B. Purves, *J. Amer. Chem. Soc.*, **61**, 755 (1939); *ibid*, **61**, 428 (1939).

(6) E. B. Whipple, *ibid*, **92**, 7183 (1970).

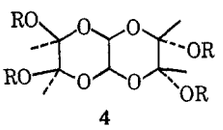
singlets at 4.98, 5.03, and 5.13 ppm for the skeletal CH protons.

In order for the six protons from the three glyoxal units to give only three equally intense lines, it is necessary that the protons occur in three equivalent pairs. Since no hyperfine splittings are apparent in the spectrum, one might naturally suspect that each equivalent pair consists of vicinal protons from a glyoxal unit in the methylated trimer. This would require that each glyoxal unit lie across a symmetry element in the molecule, and that no two of these glyoxal units be alike.

Two structures (**3** and **4**) that can satisfy these condi-



3



4

tions involve the heretofore presumed 1,4,5,8-naphthodioxane rings.

The equivalence of any pair of CH groups is removed in the ^{13}C satellite spectrum, since one of the protons will couple strongly to the directly bonded ^{13}C and the probability that the other is also attached to ^{13}C is small (the natural abundance of ^{13}C is 1.1%). One can therefore tell from the satellite spectrum whether the absence of resolvable coupling constants results from the equivalence of coupled groups.[7] This experiment, which requires time averaging to yield detectable signals, gives the result shown in Figure 1. Only one of the three ring proton lines is found to undergo additional splitting ($J_{H,H}$ = 6.76 Hz) from a vicinal proton when viewed in the ^{13}C satellite spectrum; therefore, of the three equivalent proton pairs, only one contains mutually coupled members.

Neither of the fused dioxane structures **3** or **4** is compatible with this result. The trans fused structure **3** would have two geminal proton pairs in a trans diaxial configuration, leading one to expect at least two strongly coupled pairs. A cis ring fusion would, on the other hand, require three axial–equatorial pairs, so that either all would be visibly coupled or none would be. One is forced, therefore, to abandon all the structural possibilities in which the members of all three vicinal proton pairs are equivalent and seek alternatives in which there is only one such pair, the other two glyoxal units being symmetrically located with respect to each other, but with dissimilar environments for their two CH groups. The coupling between the nonequivalent vicinial pairs must then be small by virtue of electronegative substitution and an unfavorable conformation, as in glyoxal dimer.[6,8]

A simple extension of the dioxolane structure therefore permits one to satisfy the conditions imposed by the ^{13}C satellite nmr spectrum, including reasonable agreement with the observed magnitude of the resolved vicinal coupling. There are, moreover, two such structures which correspond to a meso and racemic combination of two optically active dioxolane rings (**5** and **6**). One might therefore expect to find two diastereo-

(7) A. D. Cohen, J. Sheppard, and J. J. Turner, *Proc. Chem. Soc. London*, 118 (1958).

(8) See, however, F. A. L. Anet, *J. Amer. Chem. Soc.*, **84**, 747 (1962), where quite substantial trans vicinal couplings are observed in methyl-substituted dioxolane rings.

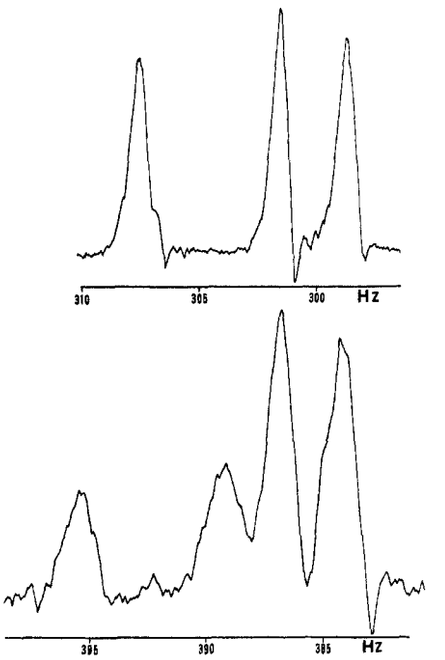
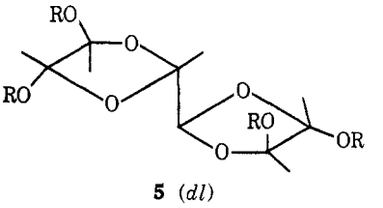
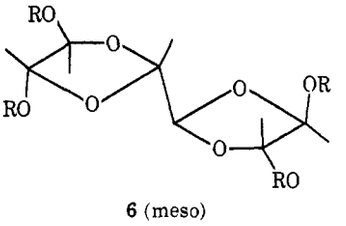


Figure 1.—Top: proton magnetic resonance spectrum (60 MHz) of skeletal protons in compound **2** in $CDCl_3$ (TMS) solution. Bottom: time averaged (300 accumulations) low-field ^{13}C satellite spectrum of the corresponding protons. The frequency scales in both spectra are referenced to tetramethylsilane.



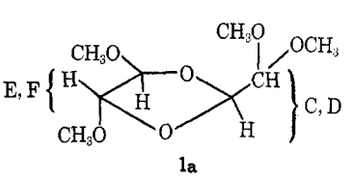
5 (*dl*)



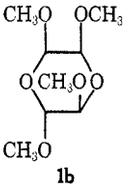
6 (meso)

isomers of compound **2**, and studies combining solvent effects and high magnetic fields do indeed permit every line in its nmr spectrum (Figure 2) to be resolved into two components present in about a 2:1 ratio (no significance can be attached to the isomer ratio which is reported here for an isolated product of the reaction). The methylated trimer can, therefore, be assigned structures **5** and **6** with confidence.

The pmr spectrum of compound **1** at 60 MHz in deuteriochloroform is shown in Figure 3. Only two structures corresponding to a tetramethoxylated dimer are compatible. These are **1a** and **1b**.



1a



1b

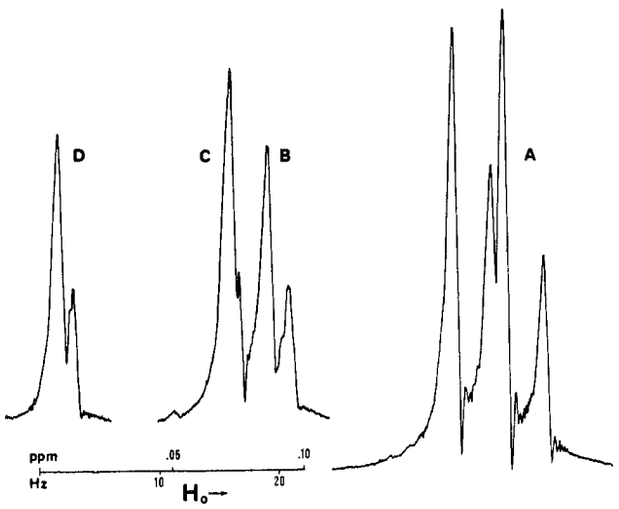
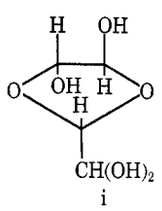


Figure 2.—Pmr absorption bands of compound **2** at 220 MHz in benzene solution, showing partially resolved lines from disastereoisomeric structures. The spectrometer gain in region A is reduced by half. The positions of the principal lines are given in Table II.

The ring proton signals C, D, E, and F of compound **1** are strikingly similar to the resonances observed for the ring protons of glyoxal dimer, which has been shown to have structure i.[6] The ring protons (E and



i

F) are nonequivalent, but are weakly coupled, as in **2** and in glyoxal dimer. Protons C and D are vicinal, nonequivalent, and favorably oriented for spin coupling, and therefore appear as a typical AB pattern. The chemical shifts of compound **1** in D_2O solution (dioxane reference) bear a simple relation to those of glyoxal dimer. Ring protons D, E, and F show incremental upfield shifts due to methoxylation of 0.0, 0.3, and 0.3 ppm, respectively, while the side-chain proton C shifts upfield by 0.6 ppm. All of the shifts are thus in accord with a simple rule that substitution of methyl groups for hydroxyl protons causes an additive, 0.3-ppm upfield shift of protons on carbon attached to the oxygen atom on which the substitution occurs, and causes negligible shifts elsewhere.

In strong magnetic fields or in pyridine solution, the methoxyl signals from compound **1** can be resolved into four lines. With increasing temperature, two of these lines approach coalescence, while the separation between the others increases very slightly, and the vicinal coupling constant between protons C and D diminishes. This behavior is typical for rotation of a group about an asymmetric environment. This fact,[9] coupled with the shape and shift similarity to glyoxal dimer, gives further support to the assignment of **1a** as the structure.

These results also suggest, but do not prove, that glyoxal trimer also consists of coupled dioxolane rings.

(9) This analysis is not conclusive; however, it is much easier to rationalize on the basis of conformational changes in **1a** than **1b**: L. M. Jackson and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Oxford Pergamon Press," London, 1969, Chapter 5-2.

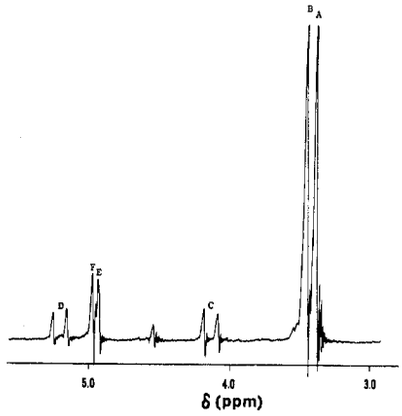


Figure 3.—Pmr spectrum (60 MHz) of compound **1** in $CDCl_3$ (TMS) solution. The line at 4.5 ppm is an impurity, suspected to be water.

An effort was therefore made to detect corresponding lines in the nmr spectrum of aqueous glyoxal solutions. One might expect to find these lines near their counterparts in glyoxal dimer, particularly in view of the earlier observation that incremental shifts on O-alkylation of the dimer were small except for CH groups attached directly to the oxygen involved. Two lines (lines 10, and 14 in reference 6) due to trimers have been reported in about the right places, and show evidence of additional structure (line 9) which is most reasonably attributed to diastereoisomeric pairs. Moreover, the spectrum of our compound **2** in D_2O solution shows a complex, single band at 1.45 ppm downfield from internal dioxane, in reasonable accord with the incremental shifts derived earlier for methoxylation of the dimer. It is also noteable that bands 10 and 14 in aqueous glyoxal are not shifted or broadened by borate salts,[6] indicating that they are due to a structure which does not contain eclipsed hydroxyl groups. It therefore appears that structures corresponding to **5** and **6** do exist as a minor component in aqueous glyoxal solutions along with at least one other trimeric species (line 16) in comparable amounts.[6]

Experimental Section[10]

A.—A mixture of 290.0 g of 80% aqueous glyoxal (4.0 mol), 1000.0 g of methyl alcohol (32.3 mol), and 182.0 g of *p*-toluenesulfonic acid (0.96 mol) in 2 l. of chloroform was heated at reflux for 4 days. No water azeotrope was observed; so the chloroform–methanol azeotrope was distilled with the addition of fresh chloroform until no more methyl alcohol was in the distillate. At that point, a water–chloroform azeotrope began to come over, and the mixture was neutralized with sodium carbonate and filtered and the water was removed by azeotropic distillation with chloroform. Distillation of the resultant product mixture through a Nester–Faust spinning-band column gave 1,1,2,2-tetrakis(methoxy)ethane, bp 83–85° (48 mm), $n^{25}D$ 1.4006 [lit.[2b,5] bp 78–79° (50 mm), $n^{25}D$ 1.4010], 271.2 g (45% yield), and 2-dimethoxymethyl-4,5-dimethoxy-1,3-dioxolane (**1**), bp 98–99° (5 mm), $n^{25}D$ 1.4225, 36.0 g (9% yield).

Anal. Calcd for $C_8H_{16}O_6$: C, 46.16; H, 7.69; mol wt, 208. Found: C, 46.23; H, 7.63, mol wt, 229.

B.—In another type of experiment, 64.0 g of methanol (2.0 mol), 72.5 g of 80% glyoxal (1.0 mol), and 2.0 g of *p*-toluenesulfonic acid (0.01 mol) were heated at reflux for 20 hr, chloroform was added, and the unreacted methanol was removed

(10) All melting and boiling points are uncorrected. Infrared spectra were measured on a Perkin-Elmer Infracord. Nmr spectra were recorded on Varian 60-MHz and 220-MHz instruments. Molecular weights were determined by Crobaugh Laboratories, Cleveland, Ohio, and microanalysis were performed by Union Carbide staff members.

azeotropically. After no more methanol was present, the water was removed azeotropically with the chloroform. The remaining chloroform was distilled away from the reaction mixture, 32.0 g of methyl alcohol (1.0 mol) was added, and the solution was brought to reflux for another 24 hr. The above procedure was then repeated and the resultant product mixture was distilled through the Nester–Faust spinning-band column to give 1,1,2,2-tetrakis(methoxy)ethane, bp 85–90° (25 mm), 6.6 g (4% yield), 2-dimethoxymethyl-4,5-dimethoxy-1,3-dioxolane (1), bp 95–98° (5 mm), 16.0 g (15% yield), and 2,2′-bis(4,5-dimethoxy-1,3-dioxolane) (2), bp 105–108° (5 mm), mp 109–110°, 17.9 g (20% yield).

Anal. Calcd for $C_{10}H_{18}O_8$: C, 45.11; H, 6.77; mol wt, 266. Found: C, 45.11; H, 6.81; mol wt, 263.

The infrared spectra of both compounds 1 and 2 showed no carbonyl or hydroxyl bonds, but had strong absorption in that region expected for ethers or acetals.

Registry No.—1, 33834-89-8; 2, 33834-90-1.

The Photochemistry of *S*-Methyl Diazothioacetate[1]

STEPHEN S. HIXSON* AND SUSAN H. HIXSON

Department of Chemistry, University of Massachusetts, Amherst, Massachusetts 01002

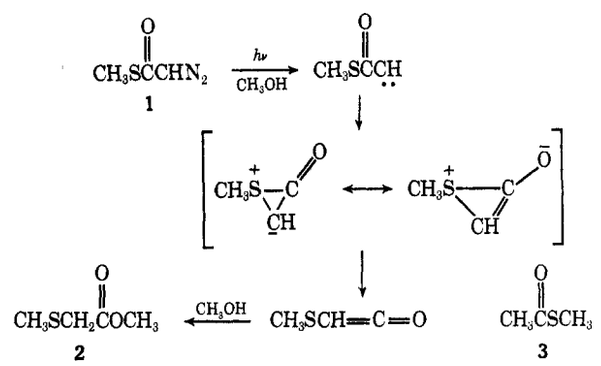
Received August 26, 1971

The photochemistry of α-diazo esters has received much attention recently both from chemists interested in the nature and mechanisms of the reactions undergone by these species[2a-e] and from others interested in using them as labeling reagents for active sites of enzymes.[3a-f] However, Wolff rearrangement of the carbenes produced upon irradiation of the diazo esters has diminished the utility of these compounds as labeling reagents, particularly in the case of diazoacetylglyceraldehyde-3-phosphate dehydrogenase[4] (only Wolff rearrangement observed) but also in diazoacetylchymotrypsin[3a,b] (15–20% rearrangement). In the former case, to date the only investigation of an α-diazothio ester, the per cent Wolff rearrangement was not determined since other products arising from, for example, solvent insertion would have gone undetected.

Since we are interested in enzyme labeling with diazo esters and because many enzymes contain the –SH group of a cysteine moiety at their active sites, we wished to examine the extent of Wolff rearrangement of an excited diazothio ester relative to oxygen (ester) and nitrogen (amide) analogs, and the effect of excited state multiplicity on the rearrangement. For these purposes the photochemistry of *S*-methyl diazothioacetate (1) has been studied.

Ester 1 was prepared in 25% yield from diazomethane and methyl chlorothiolformate. Direct photolysis of 1 in methanol with 310–380 nm light afforded in 86% yield only one detectable volatile product with a gc retention time identical with that of known methyl methylthioacetate (2). A dark control showed no reaction. The identity of the product was firmly established by distilling the final solution carefully to remove the methanol; the infrared spectrum of the remaining oil was identical with that of known 2.

The sensitized decomposition was carried out using xanthone as sensitizer and light of wavelengths 310–355 nm. Gas chromatographic analysis of the reaction mixture present when 95% of 1 had disappeared revealed only a small amount of one product with a retention time identical with that of known *S*-methyl thioacetate (3) corresponding in area to a 7% yield



from 1.[5] Benzophenone sensitization gave similar results. As expected, xanthone-sensitized decomposition of 1 in isopropyl alcohol, a better hydrogen atom donor than methanol, gave an increased yield (23%) of this product. Once again dark controls showed no loss of 1.

Assuming that the direct photolysis of 1 generates a singlet carbene, our results show that this carbene undergoes a very rapid Wolff rearrangement. No products arising from insertion into the solvent –OH bond or from hydrogen abstraction were detected by our methods of analysis. This is in contrast to the case with α-diazo esters and amides, which show a lower (20–60%) per cent rearrangement and give a significant amount of the other products.[2d] This enhanced migratory aptitude of a sulfur atom to a carbene center has also been found in carbenes generated from *p*-tosylhydrazone decomposition.[6,7]

The results of the sensitized decomposition demonstrate that multiplicity has a profound effect on the Wolff rearrangement in that the latter is eliminated entirely and only a moderate amount of what is probably the reduction product 3, presumably formed *via* stepwise hydrogen abstraction by a triplet carbene, is

(1) This work was supported by a grant (GB 27644) from the National Science Foundation and by a Faculty Research Grant from the Research Council of the University of Massachusetts, Amherst, Mass.

(2) Good leading references are (a) T. Dominh and O. P. Strausz, *J. Amer. Chem. Soc.*, **92**, 1766 (1970); (b) D. E. Thornton, R. K. Gosavi, and O. P. Strausz, *ibid.*, **92**, 1768 (1970); (c) W. Ando, *et al.*, *J. Org. Chem.*, **36**, 1732 (1971); (d) H. Chaimovich, R. J. Vaughan, and F. H. Westheimer, *J. Amer. Chem. Soc.*, **90**, 4088 (1968); (e) G. O. Schenck and A. Ritter, *Tetrahedron Lett.*, 3189 (1968).

(3) (a) A. Singh, E. R. Thornton, and F. H. Westheimer, *J. Biol. Chem.*, **237**, 3006 (1962); (b) J. Schafer, P. Baronowsky, R. Laursen, F. Finn, and F. H. Westheimer, *ibid.*, **241**, 421 (1966); (c) R. J. Vaughan and F. H. Westheimer, *J. Amer. Chem. Soc.*, **91**, 217 (1969); (d) D. T. Browne, S. S. Hixson, and F. H. Westheimer, *J. Biol. Chem.*, **246**, 4477 (1971). (e) C. Hexter and F. H. Westheimer, *ibid.*, **246**, 3928, 3934 (1971); (f) see also R. R. Rando, *J. Amer. Chem. Soc.*, **92**, 6706 (1970).

(4) J. H. Scott, unpublished results, Harvard University, 1965. Part of this work is cited in ref 2d.

(5) Due to the high absorption of 1 and the low solubility of sensitizer, it was necessary to use a dilute solution containing a relatively large amount of sensitizer in the presence of a very small amount of 1 in order to ensure complete absorption of light by the sensitizer. This precluded an extensive search for unknown products.

(6) J. H. Robson and H. Schechter, *J. Amer. Chem. Soc.*, **89**, 7112 (1967).

(7) Wolff rearrangement *via* an oxirene formation–hydrogen shift sequence, a minor process in diazo ester photolysis (vapor phase),[2b] seems unlikely in the present case, but it cannot be ruled out.