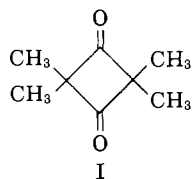## Primary Processes in the Photochemistry of Tetramethyl-1,3-cyclobutanedione

*Sir:*

In two[1,2] recent communications it has been postulated that the photolysis of tetramethyl-1,3-cyclobutanedione (I) gives tetramethylcyclopropanone and carbon

monoxide through a photochemical primary process (1). The evidence that was presented was entirely

$$I + h\nu \longrightarrow \text{(tetramethylcyclopropanone)} + CO \qquad (1)$$
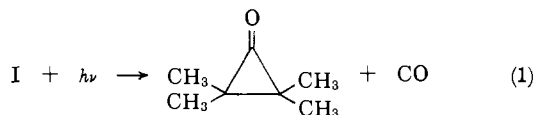
indirect. The evidence in a third communication[3] suggested that decomposition to give 2 molecules of dimethylketene (2) also occurred in 15–20% of the

$$I + h\nu \longrightarrow 2(CH_3)_2C{=}C{=}O \qquad (2)$$
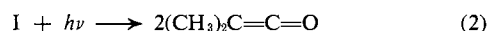
molecules of I that were photolyzed. It is the purpose of this communication to present data that show the rather complex photochemical relationships that exist in this system.

Photolyses of I in cyclohexane solution were carried out in a cell with KBr windows at room temperature, while the photolyses of I in a nitrogen matrix were conducted at 4°K. In either case it was possible to scan the infrared spectrum of the photolysate with a delay of a few minutes or less. Ultraviolet spectra of the photolysate were also obtained when the experiments were carried out at room temperature. The conversion of I was held to 10% or less to ensure that secondary photodecomposition of the products did not occur.

On irradiation of I, both in solution and in the matrix, two intense absorption peaks were observed, at 1840 and at 2124 cm.$^{-1}$. The latter was due to dimethylketene while the former can reasonably be attributed to the carbonyl stretch frequency in tetramethylcyclopropanone.[4] Weak absorptions at 2137 (CO) and 1820 cm.$^{-1}$ (—CO—O—CO—?)[5] were also observed. From pure samples of dimethylketene it was possible to determine the extinction coefficient for the absorption at 2124 cm.$^{-1}$. In this manner, the fraction of I that decomposed by reaction 2 at room temperature, in cyclohexane, was estimated to be *at least* 0.2, in reasonable agreement with the earlier result.[3] Exactly the same value was obtained from the ultraviolet spectrum of the photolysate as well. This value was not affected by changes in the incident wave length from 3100 to 2500 Å.

The presence of primary process 2 severely compli-

(1) H. G. Richey, Jr., J. M. Richey, and D. C. Clagett, *J. Am. Chem. Soc.*, 86, 3906 (1964).

(2) P. A. Leermakers, G. F. Vesley, N. J. Turro, and D. C. Neckers, *ibid.*, 86, 4213 (1964).

(3) N. J. Turro, G. W. Byers, and P. A. Leermakers, *ibid.*, 86, 955 (1964).

(4) W. B. DeMore, H. O. Pritchard, and N. Davidson, *ibid.*, 81, 5874 (1959).

(5) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p. 127. This band was also observed when the solution of dimethylketene in cyclohexane was allowed to react with water.

cates the photochemistry of I in two different ways. The ultraviolet spectrum of dimethylketene indicates a weak absorption at 4000 Å. and an intense one at 2500 Å.[6] Since I itself absorbs only weakly or not at all at these wave lengths, it follows that secondary photolysis of dimethylketene can be avoided only if monochromatic radiation absorbed only by I is used. Thus a quantum yield for the formation of carbon monoxide from I at 3660 Å.[3] is likely to have a contribution from the photolysis of dimethylketene. It was also observed in this study that: (1) The photolysis of dimethylketene in cyclohexane at 2537 Å. gave carbon monoxide and tetramethylethylene as products. In addition the presence of an absorption at 1840 cm.$^{-1}$ in the solution was attributable only to tetramethylcyclopropanone. Since the conversion of the reactant was negligibly small, the products could have come only from dimethylketene. (2) On bubbling oxygen through a solution of dimethylketene in cyclohexane, the absorption peak at 2124 cm.$^{-1}$ diminished gradually while absorptions at 2334 (CO_2) and 1720 cm.$^{-1}$ (acetone) became apparent. This is in accordance with the earlier observations of Staudinger.[7] (3) The ultraviolet irradiation of dimethylketene in a nitrogen matrix at 4°K. did not lead to any apparent decomposition.

It has already been stated that the compound which, in the photolysis of I, gave rise to an infrared absorption at 1840 cm.$^{-1}$ was tentatively identified as tetramethylcyclopropanone. This constitutes the most direct evidence to date for the formation of this product in this system. The generation of the same absorption in photolysis of dimethylketene in solution can be explained by the reactions[8]
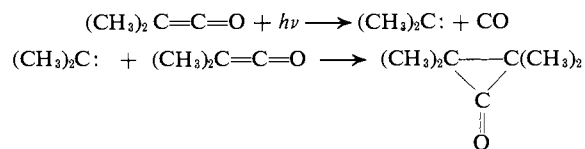
$$(CH_3)_2C{=}C{=}O + h\nu \longrightarrow (CH_3)_2C{:} + CO$$

It was interesting to note that, in a solution of I that had been partially photolyzed, the absorption at 2124 cm.$^{-1}$ (($CH_3)_2C{=}C{=}O$) disappeared readily when oxygen was bubbled in, while the absorption at 1840 cm.$^{-1}$ diminished only slowly and did not disappear completely under the same conditions. On standing overnight at room temperature in the absence of oxygen, both absorptions decreased, the one at 1840 cm.$^{-1}$, however, at a much higher rate.

The extent to which primary process 1 takes place is hard to estimate since the properties of a pure sample of tetramethylcyclopropanone are not known. If the extinction coefficient for the carbonyl frequency of this compound is taken to be the same as that for cyclobutanone, primary process 1 can account for the disappearance of only as much I as primary process 2. It is interesting to speculate if there is yet a third process which can be written as

$$I + h\nu \longrightarrow \text{(tetramethylethylene)} + 2CO \qquad (3)$$
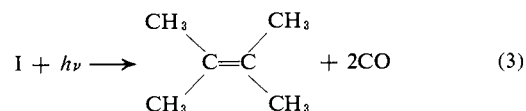
(6) R. A. Holroyd and F. E. Blacet, *J. Am. Chem. Soc.*, 79, 4830 (1957).

(7) H. Staudinger, K. Dyckerhoff, H. W. Klever, and L. Ruzicka, *Ber.*, 58, 1083 (1925).

(8) These reactions are analogous to the addition of methylene to ketene to give cyclopropanone (ref. 4).

Earlier indications[1,2] of the importance of (1), which rely on the formation of a hemiketal of tetramethylcyclopropanone, are unreliable since the solvent may very well complex with I in the excited state and thus promote the monodecarbonylation reaction.[9]

The reactions in this system can be summarized as
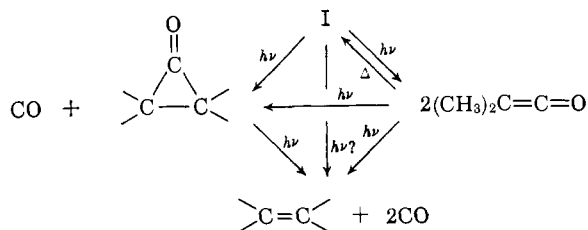
(9) E. M. Kosower, J. Chem. Phys., 38, 2813 (1963).

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The Direct Preparation of 2'-O-Methyladenosine from Adenosine[1]

Sir:

Smith and Dunn[2] isolated a compound from the RNA of wheat germ and rat liver which they designated as 2'- (or 3'-) O-methyladenosine. This compound isolated from yeast soluble RNA was identified as 2'-O-methyladenosine (I) by Hall,[3] based on chromatographic comparison of hydrolysis products with authentic 2-O-methyl-D-ribose. 2'-O-Methyladenosine (I) and other 2'-O-methylribonucleoside derivatives of the naturally occurring heterocyclic bases have been found in both soluble and high molecular weight RNA from a variety of sources.[4-8]

We wish to report the first chemical synthesis of a naturally occurring 2'-O-methylpurineribonucleoside, 6-amino-2'-O-methyl-9-β-D-ribofuranosylpurine (2'-O-methyladenosine, I). Adenosine has been methylated selectively on the adenine moiety with methyl iodide in the absence of strong base to give 1-methyladenosine in good yield.[9] Szer and Shugar[10] report that excess diazomethane and uridylic acid result in a small amount of product which is methylated in the ribose moiety as well as at nitrogen 3. It has been reported[11] that adenosine methylates only very slowly in neutral aqueous media with ethereal diazomethane to give 1-methyladenosine. In an effort to obtain selective O-methylation, the reaction of diazomethane on adenosine in a homogeneous solution of water and 1,2-dimethoxyethane was studied. Under these con-

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(3) R. H. Hall, ibid., 68, 278 (1963).
(4) R. H. Hall, Biochem. Biophys. Res. Commun., 12, 429 (1963).
(5) B. B. Biswas and J. Meyers, Nature, 186, 238 (1960).
(6) S. Morisawa and E. Chargaff, Biochim. Biophys. Acta, 68, 147 (1963).
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(8) R. H. Hall, Biochemistry, 3, 876 (1964).
(9) J. W. Jones and R. K. Robins, J. Am. Chem. Soc., 85, 193 (1963).
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ditions the 2'-hydroxyl was found to react preferentially to give a good yield of 2'-O-methyladenosine. To 5 g. of adenosine monohydrate dissolved in 200 ml. of warm (80°) water was added all at once, with stirring, a solution of 25 g. of diazomethane dissolved in 500 ml. of 1,2-dimethoxyethane. The clear yellow solution was allowed to cool to room temperature and was stirred overnight, at which time the color was discharged. The solution was reduced *in vacuo* to a heavy sirup. The sirup was dissolved in aqueous ethanol (80%) and evaporated *in vacuo*. This process was repeated several times with absolute ethanol to give a white foam which contained adenosine and 2'-O-methyladenosine in approximately equal quantities and a small amount of an unidentified fast moving spot, as judged by paper chromatography. The crude product was purified by column partition chromatography using the sodium borate–butanol–celite system described by Hall.[8] Fractions 5–9 were reduced to dryness to give 2.0 g. (41%) of a chromatographically pure white solid which was recrystallized from absolute ethanol to give a product (I), m.p. 200–202°; $[\alpha]^{24}D$ −58.2° (c 1, H_2O). Anal. Calcd. for $C_{11}H_{15}N_5O_4$: C, 47.0; H, 5.34; N, 24.9. Found: C, 47.1; H, 5.67; N, 25.0. Rigorous comparison[12] of synthetic 2'-O-methyladenosine with the natural material in four solvent systems showed the products to be identical (Table I). In addition, the two samples were

Table I

System	Solvent	R
1.	1-Butanol–water–concd. ammonia, 86:14:5	0.49
2.	2-Propanol–concd. HCl–water, 680:170:144	0.53
3.	2-Propanol–water–concd. ammonia 7:2:1	0.71
4.	Ethyl acetate–1-propanol–water 4:1:2	0.57

electrophoresed at pH 9.2 under two conditions: (1) in 0.05 M glycine buffer and (2) in 0.05 M glycine–0.05 M borate buffer. In both buffers the two samples migrated 5.5 cm. toward the negative pole (22 v./cm. for 4 hr.) A proton magnetic resonance spectrum in dimethyl-d_6 sulfoxide showed a sharp singlet (3H) at δ 3.78 due to the 2'-O-methyl group (TMS as an external standard). Ultraviolet absorption spectral data gave peaks at $\lambda_{max}^{pH\ 1}$ 256.5 mμ (ϵ 13,800), λ_{max}^{MeOH} 258.5 mμ (ϵ 13,700), and $\lambda_{max}^{pH\ 11}$ 258.5 mμ (ϵ 13,900). Acid hydrolysis gave adenine and 2'-O-methyl-D-ribose which were identified by rigorous chromatographic comparison in three solvent systems with authentic adenine and synthetic 2'-O-methyl-D-ribose.[13] Treatment of 2'-O-methyladenosine (I) with sodium nitrite and acetic acid in the presence of a small amount of 1 N hydrochloric acid, after standing for 3 days at room temperature, gave 2'-O-methylinosine (II) in 58% yield. Recrystallization of II from 98% ethanol gave needles, m.p. 177–180°; $\lambda_{max}^{pH\ 1}$ 248 mμ (ϵ 14,100) and $\lambda_{max}^{pH\ 11}$ 251 mμ (ϵ 15,000). Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.3; H, 4.96; N, 19.8. Found: C, 46.5; H, 5.12; N, 20.0.

(12) The authors wish to thank Dr. R. H. Hall for this direct comparison of our 2'-O-methyladenosine with the natural product isolated from his laboratory.
(13) J. Sowden, M. Oftedahl, and A. Kirkland, J. Org. Chem., 27, 1741 (1962).