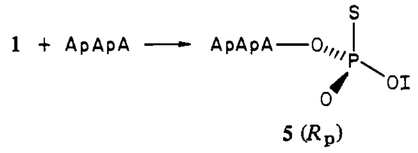
Scheme IV



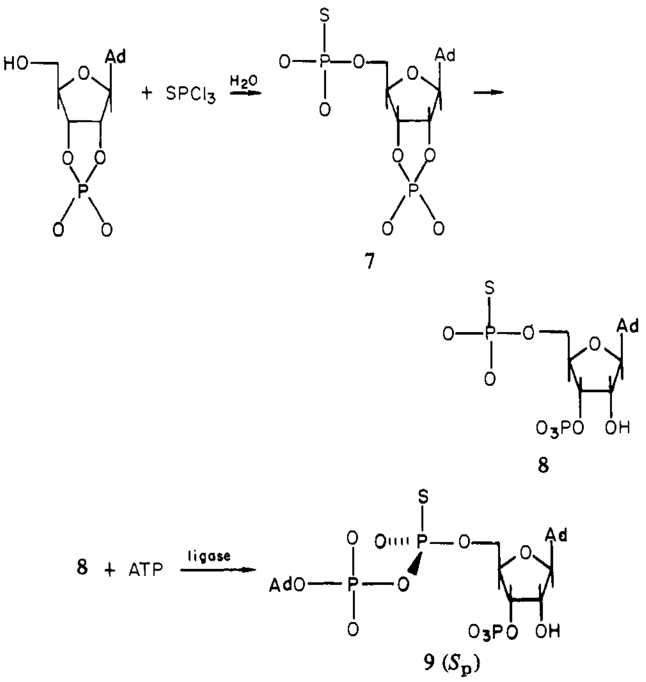
cellulose[7] in >95% isomeric purity.[8]

Determination of the absolute stereochemistry at the thiophosphoryl center in **1** and **2** was achieved via the sequence illustrated for **1** in Scheme III. Compounds **3** (IDPαS) and **4** (ADPβS) were cleanly separated by column chromatography on DEAE-Sephadex A-25.[9] The IDPαS derived from **1** was reactive in a pyruvate kinase–lactate dehydrogenase couple whereas the IDPαS derived from **2** was unreactive. Since this enzyme couple is specific for an α-thiophosphoryl of S_p configuration,[10] **1** and **2** have absolute configurations as written. The design of **1** and **2** was predicated by earlier experiments that demonstrated dinucleotide pyrophosphates would substitute for App(Np)$_n$ in step 3 of Scheme I and that AMP is strongly favored as the leaving group.[11]

Incubation of either **1** or **2** in the presence of ApApA and ligase at pH 8.3[11] revealed that **1** but not **2** yielded the oligoribonucleotide product, ApApAp(S)I (**5**). The product was isolated on DEAE-Sephadex A-25[12] and identified by UV spectroscopy [λ_{max} 255 nm, λ_{max} (predicted) 254.9 nm], position of elution, and digestion by spleen diesterase which gave 3′-AMP and Ap(S)I.[13] The absolute stereochemistry of the thiophosphoryl linkage was established by its cleavage in the presence of venom phosphodiesterase at a rate comparable to that for Ap(S)A (R_p).[14] Under identical conditions the Ap(S)A (S_p) dinucleotide was not degraded. Since the stereochemistry of **5** is R_p at the Ap(S)I linkage, step 3 of the ligase reaction proceeds with inversion of configuration and is consistent with a direct displacement process (Scheme IV).

The stereochemical course of step 2 was traced by employing p(S)Ap (**8**)—step 2 requires a 3′-phosphate when n = 1[15]—synthesized from cyclic 2′,3′-AMP and thiophosphoryl chloride[16] followed by acid hydrolysis (0.1 M HCl) to give a mixture of 2′ and 3′ isomers.[17] Incubation of the mixture (2′ isomer is noninhibitory) in the presence of ligase and ATP, pH 7.2,[18] proceeds to form App(S)Ap (**9**) as shown in Scheme V.

Scheme V



The structure of **9** was inferred by alkaline phosphatase catalyzed hydrolysis to App(S)A, which was isolated by DEAE-Sephadex A-25 column chromatography.[19] The absolute stereochemistry of App(S)A was obtained by comparison to authentic samples obtained via Scheme II except with adenosine substituted for inosine and shown to have the S_p configuration.[20] Thus the absolute configuration at the reacting phosphoryl center is the same in both steps.

The ligation in step 3 is identical in terms of its inversion stereochemical course with other displacements at phosphoric diesters[21] with the exception of the retention stereochemistry noted for venom[14,22] and intestinal phosphodiesterases.[23] Moreover the S_p absolute configuration at the thiophosphoryl center is generally preferred in reactions that maintain a diester linkage after the displacement. These results suggest the possibility of common active-site and mechanistic features linking polymerization, ligation, and transfer reactions. The ability to introduce a thiophosphoryl center into RNA also should furnish us with a sensitive probe of RNA structure.

Acknowledgment. We thank Professor O. Uhlenbeck for his advice and generous gift of T4 RNA ligase.

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[7] Separated by a linear gradient (0.1–0.5 M) of $(NH_4)HCO_3$. For resolution of the isomers a second column employing a similar gradient was required.

[8] **1** (S_p): δ(PS) 44.0, δ(PO) −11.2 downfield from H_3PO_4. **2** (R_p): δ(PS) 44.2, δ(PO) −11.2 downfield from H_3PO_4. J_{PS-PO} = 28.5 ± 1 Hz for both compounds. λ_{max} 252 nm (ε 21 300) for **1** and **2**.

[9] Separated by a linear gradient (0.1–0.85 M) of $[(C_2H_5)_3NH]HCO_3$. Peak assignments were based on λ_{max} 248 nm for **3** and λ_{max} 258 nm for **4**. Compound **3** gave a single spot on TLC (poly(ethylenimine)–cellulose) eluted with 0.75 M KH_2PO_4, pH 3.5.

[10] F. Eckstein and R. S. Goody, *Biochemistry*, **15**, 1685–1691 (1976). We are presuming the substitution of inosine for adenosine does not alter the enzyme couple's specificity.

[11] T. E. England, R. I. Gumport, and O. C. Uhlenbeck, *Proc. Natl. Acad. Sci. U.S.A.*, **74**, 4839–4842 (1977).

[12] A linear gradient (0.1–0.9 M) of $[(C_2H_5)_3NH]HCO_3$ was employed.

[13] These products were chromatographed by TLC (poly(ethylenimine)–cellulose) eluted with 0.75 M KH_2PO_4, pH 3.5, and compared to standards.

[14] F. R. Bryant and S. J. Benkovic, *Biochemistry*, **18**, 2825–2828 (1979).

[15] (a) Y. Kikuchi, F. Hishinuma, and K. Sakaguchi, *Proc Natl. Acad. Sci. U.S.A*, **75**, 1270–1273 (1978). (b) T. E. England and O. C. Uhlenbeck, *Biochemistry*, **17**, 2069–2076 (1978).

[16] **7**: δ(PS) 43.2; δ(PO) 19.2 downfield from H_3PO_4.

[17] Alternatively, digestion of **7** with RNase T_2 yields only the 3′ isomer.

[18] O. Uhlenbeck, personal communication.

[19] A linear gradient (0.1–0.7 M) of $(NH_4)HCO_3$ was used.

[20] S_p, δ(PS) 43.3, δ(PO) −11.9 downfield from H_3PO_4 for **1** where inosine is replaced by adenosine. R_p, δ(PS) 43.6, δ(PO) −11.9 downfield from H_3PO_4 for **2** where inosine is replaced by adenosine. J_{PS-PO} = 27.7 ± 2 Hz for both compounds. The diastereomers were identified by comparing these parameters with the parameters previously reported by Richards, J. P., et al. [*J. Am. Chem. Soc.*, **100**, 7756–7757 (1978)] and with those reported for the S_p and R_p diastereomers of **1** and **2** in ref 8.

[21] J. R. Knowles, *Annu. Rev. Biochem.*, **49**, 877–919 (1980).

[22] P. M. J. Burgers, F. Eckstein, and D. H. Hunneman, *J. Biol. Chem.* **254**, 7476–7478 (1979).

[23] F. R. Bryant, J. F. Marlier, and S. J. Benkovic, "Phosphorus Chemistry Directed Towards Biology", W. J. Stec, Ed., Pergamon Press, Oxford, 1980, pp 129–131.

Mechanistic Photochemistry of Acylsilanes. 1. Reaction with Alcohols

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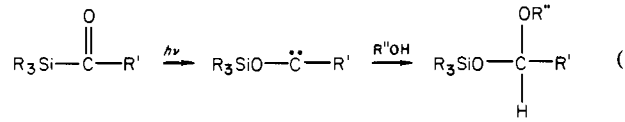
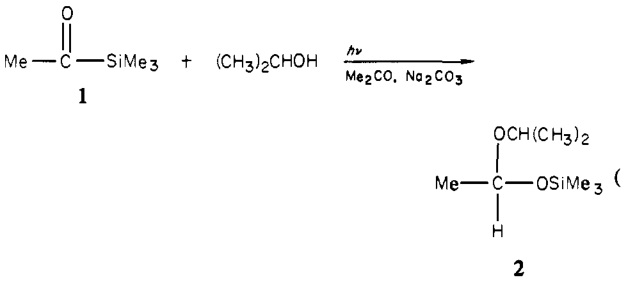
In recent years the exploratory photochemistry of acylsilanes (α-silyl ketones) has generated considerable interest.[1-3] Brook has postulated that the important primary photochemical processes for acylsilanes ($R'_3Si(R)C{=}O$) are (a) rapid migration of silicon from carbon to oxygen to generate a nucleophilic siloxycarbene ($R-\ddot{C}-OSiR'_3$) which undergoes intermolecular reaction with a variety of reagents in competition with rearrangement to ground-state acylsilane and (b) relatively slow cleavage of the carbonyl carbon-α-silicon bond to generate silyl and acyl radicals.[1-3] For example, Brook and Duff showed that acylsilanes/ irradiated in alcohols yield acetals. They postulated that the reaction involves initial isomerization of the acylsilane to a siloxycarbene, followed by insertion of the carbene in the O–H bond (eq 1).[2]



$$R_3Si-C(=O)-R' \xrightarrow{h\nu} R_3SiO-\ddot{C}-R' \xrightarrow{R''OH} R_3SiO-C(OR'')(H)-R' \quad (1)$$

We have investigated the mechanism and excited-state origin of this reaction as part of a broad and detailed study of the mechanistic photochemistry of acylsilanes. We were particularly interested in (a) determining whether the acylsilane to siloxycarbene rearrangement was occurring from the acylsilane S_1 and/or T_1 state and (b) ruling out the possibility that acetal resulted from direct reaction of the acylsilane S_1 and/or T_1 state with alcohols.

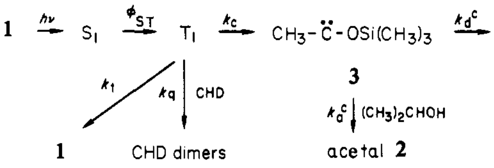
Acetyltrimethylsilane (**1**) and 2-propanol were chosen for study as a model system. Irradiation of **1** at 366 nm in neat 2-propanol or in an acetone solution of 2-propanol (both stabilized by added sodium carbonate) gives acetal **2** as the sole photoproduct in 80–90% yield (eq 2).



$$\underset{\mathbf{1}}{Me-C(=O)-SiMe_3} + (CH_3)_2CHOH \xrightarrow[Me_2CO,\ Na_2CO_3]{h\nu} \underset{\mathbf{2}}{Me-C(OCH(CH_3)_2)(H)-OSiMe_3} \quad (2)$$

The following observations clearly indicate that formation of acetal **2** results from reaction of 2-propanol with the acylsilane T_1 state and/or siloxycarbene derived from rearrangement of the acylsilane T_1 state: (1) Acetophenone (E_T = 74 kcal/mol[4]) sensitizes reaction of acetyltrimethylsilane (E_T = 61 kcal/mol)[5] with alcohol.[6] (2) 1,3-Cyclohexadiene (CHD, 0.4 M, E_T = 54 kcal/mol[7]) quenches >99% of acetal formation from irradiation of acylsilane **1** in neat 2-propanol. (3) 1,3-Cyclohexadiene (0.4 M) quenches only 20% of the fluorescence of **1**.[8] (4) Irradiation of acetyltrimethylsilane (**1**) with 1,3-cyclohexadiene in the absence of 2-propanol results in smooth production of diene dimers as the sole photoproducts;[9] no photochemical reaction between acylsilane **1** and 1,3-cyclohexadiene was observed. These observations eliminate the possibility of the acylsilane S_1 state or any species, such as siloxycarbene, derived from the S_1 state reacting with 2-propanol to give measurable amounts of the acetal.

Scheme I



The remaining question is whether acetal **2** is formed via reaction of 2-propanol directly with the acetyltrimethylsilane T_1 state or with some species (presumably siloxycarbene) formed from the T_1 state. This can be easily answered. If alcohol reacts directly with T_1, then the lifetime, τ_T, of the acylsilane triplet state must decrease with increasing alcohol concentration. On the other hand, if 2-propanol reacts only with the siloxycarbene, then τ_T for the acylsilane T_1 state will be independent of alcohol concentration.[10]

We have determined the triplet lifetime for acetyltrimethylsilane in the presence of varying 2-propanol concentrations by Stern–Volmer treatments of 1,3-cyclohexadiene quenching of formation of acetal **2**. The relevant kinetic expression is shown in eq 3 where

$$\Phi_{ac}{}^0/\Phi_{ac} = 1 + k_q\tau_T[\mathrm{CHD}] \qquad (3)$$

$\Phi_{ac}{}^0$ and Φ_{ac} are the quantum yields for acetal formation in the absence and presence of 1,3-cyclohexadiene, respectively, k_q is the bimolecular rate constant for quenching of the acylsilane T_1 state by 1,3-cyclohexadiene, and τ_T is the acylsilane triplet lifetime. The slopes ($k_q\tau_T$) of the Stern–Volmer plots for 2-propanol concentrations of 0.54 M, 1.3 M, and 3.9 M are constant within experimental error ($k_q\tau_T = 258 \pm 15$). A value of 2.0×10^{10} M^{-1} s^{-1} for k_q in acetone[11] yields a τ_T value of 1.29×10^{-8} s. Clearly the acetyltrimethylsilane triplet lifetime does *not* decrease with increasing 2-propanol concentration,[12] and thus the acylsilane T_1 state is not reacting with 2-propanol. Therefore acetal formation must result from reaction of alcohol with an intermediate generated from the acylsilane triplet state. As suggested by Brook,[2] siloxycarbene **3** is a very reasonable candidate for this species, giving the mechanism for acetal formation shown in Scheme I, where Φ_{ST} is the intersystem crossing quantum yield.

Further support for this mechanism is provided by our observation that addition of 2-propanol to benzene solutions of acetyltrimethylsilane and 1,3-cyclohexadiene (0.07 M), followed by photolysis, results in formation of acetal **2** but does *not* quench cyclohexadiene dimer formation. This again indicates that 2-propanol and cyclohexadiene interact with different species, the siloxycarbene with 2-propanol and the acylsilane T_1 state with cyclohexadiene.

Additional interesting kinetic information about this system can be obtained from studying the dependence of the quantum yield for acetal formation, Φ_{ac}, on the 2-propanol concentration in the absence of diene ([CHD] = 0). The appropriate expression, derived from Scheme I, is given in eq 4 where Φ_c is the efficiency

$$\begin{gathered}\Phi_{ac}{}^{-1} = \Phi_{ST}{}^{-1}\Phi_c{}^{-1}(1 + (k_d{}^c/k_a{}^c[\mathrm{ROH}])) \\ \Phi_c = k_c/(k_c + k_1)\end{gathered} \qquad (4)$$

of siloxycarbene formation from the acylsilane T_1 state and ROH

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(1) For reviews see: (a) Brook, A. G. *Intra-Sci. Chem. Rep.* **1973**, *7*, 131. (b) Brook, A. G. *Adv. Organomet. Chem.*, **1968**, *7*, 95.

(2) (a) Brook, A. G., Duff, J. M. *J. Am. Chem. Soc.* **1967**, *89*, 454. (b) Duff, J. M.; Brook, A. G. *Can. J. Chem.* **1973**, *51*, 2869.

(3) See, for example: (a) Brook, A. G.; Kucera, H. W.; Pearce, R. *Can. J. Chem.* **1971**, *49*, 1618. (b) Brook, A. G.; Pearce, R.; Pierce, J. B. *Ibid.* **1971**, *49*, 1622. (c) Brook, A. G.; Pierce, J. B.; Duff, J. M. *Ibid.* **1975**, *53*, 2874. (d) Brook, A. G.; Duff, J. M. *J. Am. Chem. Soc.* **1969**, *91*, 2118. (e) Brook, A. G.; Dillon, P. J.; Pearce, R. *Can. J. Chem.* **1971**, *49*, 133. (f) Porter, N. A.; Iloff, P. M., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 6200. (g) Brook, A. G.; Duff, J. M. *Can. J. Chem.* **1973**, *51*, 352. (h) Watanabe, H.; Kogure, T.; Nagai, Y. *J. Organomet. Chem.* **1972**, *43*, 285. (i) Watanabe, H.; Ohsawa, N.; Sawai, M.; Kukasawa, Y.; Matsumoto, H.; Nagai, Y. *Ibid.* **1975**, *93*, 1973. (j) Hassner, A.; Soderquist, J. A. *Tetrahedron Lett.* **1980**, 429.

(4) Murov, S. L. "Handbook of Photochemistry"; Marcel Dekker: New York, 1973; p 3.

(5) Dalton, J. C.; Evitt, E. R., unpublished results.

(6) This reaction was done with methanol in order to minimize intermolecular hydrogen abstraction from the alcohol by the acetophenone $^3n,\pi^*$ state.

(7) Turro, N. J. "Modern Molecular Photochemistry"; Benjamin/Cummings: Menlo Park, CA, 1978; p 353.

(8) The $k_q\tau_S$ value for CHD quenching of acetyltrimethylsilane fluorescence is 0.6.

(9) Valentine, D.; Turro, N. J.; Hammond, G. S. *J. Am. Chem. Soc.* **1964**, *86*, 5202.

(10) In this case the only way the acylsilane triplet lifetime could depend on the alcohol concentration would be if the siloxycarbene was in equilibrium with the acylsilane triplet state. This seems an unlikely possibility.

(11) This is the diffusion-controlled rate (k_{diff}) in acetone calculated from $k_{diff} = 8RT/3000\eta$ by using a value of 0.32 cP for the viscosity (η) of acetone at 25 °C. See: (a) Calvert, J. G.; Pitts, J. N., Jr. "Photochemistry"; Wiley: New York, 1966; p 626. (b) "Handbook of Chemistry and Physics", 54th ed.; Weast, R. C., ed., Chemical Rubber Publishing Co.: Cleveland, 1973; p F50.

(12) Correction of k_q for increases in viscosity with increasing 2-propanol concentration could lead to small increases in τ_T.

is 2-propanol. Plotting Φ_{ac}^{-1} vs. [2-propanol]$^{-1}$ yields a straight line with a slope of 6.9 and an intercept of 1.6, indicating that $\Phi_{ST}\Phi_c$ equals 0.63 while k_a^c/k_d^c is 0.23. We have estimated Φ_{ST} for acylsilane **1** to be 0.9 by using the sensitized dimerization of cyclohexadiene for triplet counting.[9,13] With the τ_T value determined above this allows us to estimate the efficiency ($\Phi_c = 0.70$) and the rate constant ($k_c = 5.4 \times 10^7$ s^{-1}) for formation of siloxycarbene from the acylsilane T_1 state.[14] The ratio of the rate constants for reaction of siloxycarbene **3** with 2-propanol and rearrangement of siloxycarbene **3** to acylsilane **1** ($(k_a^c/k_d^c) = 0.23$) clearly demonstrates that reversion of siloxycarbene to ground-state acylsilane is sufficiently facile that relatively high concentrations of 2-propanol are required for efficient trapping of the siloxycarbene.

In summary, we have shown that acetal formation upon irradiation of acylsilane **1** in the presence of 2-propanol occurs exclusively via reaction of alcohol with an intermediate, presumably siloxycarbene **3**, formed from the acylsilane T_1 state.[15] We are actively engaged in pursuing the generality of this conclusion with respect to other acylsilane photoreactions.[16]

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, the National Science Foundation, and the Bowling Green State University Faculty Research Committee for support of this research.

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[13] Vesley, G. F.; Hammond, G. S. *Mol. Photochem.* **1973**, *5*, 367.

[14] If siloxycarbene formation involves initial α-cleavage this would be the α-cleavage rate constant.

[15] We have no definitive evidence at present on the multiplicity (singlet or triplet) of the siloxycarbene state which reacts with alcohol.

[16] See: (Dalton, J. C.; Bourque, R. A. *J. Am. Chem. Soc.* **1981**, following paper in this issue) for an interesting example of an acylsilane photoreaction that does not involve siloxycarbene intermediates.

Mechanistic Photochemistry of Acylsilanes. 2. Reaction with Electron-Poor Olefins

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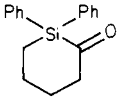
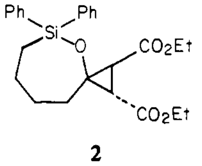
Received September 2, 1980

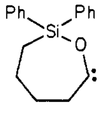
In 1971 Brook and co-workers reported that irradiation of silacyclohexanone **1** in diethyl fumarate results in the formation of the spirocyclopropane **2**.[1] This was taken at the time quite reasonably as prima facie evidence for the formation of siloxycarbene **3** in the photolysis of **1** and was thereby supportive of Brooks's general proposal that a number of acylsilane photoreactions occur via initial formation of a nucleophilic siloxycarbene intermediate.[1-3] Our interest in the photoreaction of acylsilanes and electron-poor olefins was prompted in part by an observation that *trans*-1,2-dicyanoethylene quenches the excited singlet state of simple acyclic acylsilanes with a bimolecular rate constant close to the diffusion-controlled limit.[4] This suggested the interesting possibility that cyclopropane formation might result from reaction of the electron-poor olefin with an acylsilane excited state rather than with a siloxycarbene.



1

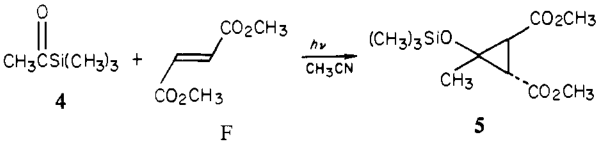


2



3

The photoreaction of acetyltrimethylsilane (**4**) with dimethyl fumarate (F) was chosen for study as a model system. Irradiation of acylsilane **4** in the presence of F leads in good yield to a single photoproduct, the *trans*-cyclopropane **5** (eq 1). No cis–trans isomerization of the fumarate is observed. Interestingly, the photoreaction of **4** with the *cis*-olefin, dimethyl maleate, is nonstereospecific, yielding a 3:2 mixture of *trans*- and *cis*-cyclopropanes, respectively.[5] We describe here experiments designed to determine the identity (S_1, T_1, siloxycarbene formed from S_1, and/or siloxycarbene formed from T_1) of the species, generated on irradiation of acylsilane **4**, which reacts with F to form cyclopropane **5**. The accompanying manuscript[6] demonstrates that acetal formation on irradiation of acylsilane **4** with 2-propanol occurs via reaction of the alcohol with a siloxycarbene formed by rearrangement of the acylsilane T_1 state. This information will be useful to us in unraveling the mechanism for cyclopropane formation.



(1)

The following observations clearly indicate that cyclopropane formation in the photoreaction of acylsilane **4** with F does *not* involve reaction of a siloxycarbene intermediate with the electron-poor olefin but rather results from direct reaction of F with both the acylsilane S_1 and T_1 states.

(1) Concentrations of 2-propanol up to 10 M have no effect on the quantum yield for cyclopropane formation from acylsilane **4** and F ([F] ≥ 0.002 M). Acetal, from reaction of siloxycarbene ($(CH_3)_3Si\ddot{O}CCH_3$) with 2-propanol,[6] is observed under these conditions. This observation demonstrates that the siloxycarbene responsible for reaction with 2-propanol to yield acetal is *not* reacting with F to yield cyclopropane.[7]

(2) Benzophenone (E_T = 69 kcal/mol[8a]) sensitization of reaction

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[1] Brook, A. G.; Kucera, H. W.; Pearce, R. *Can. J. Chem.* **1971**, *49*, 1618.

[2] For reviews see: (a) Brook, A. G. *Intra-Sci. Chem. Rep.* **1973**, *7*, 131: (b) Brook, A. G. *Adv. Organomet. Chem.* **1968**, 7, 95.

[3] See, for example: (a) Brook, A. G.; Kucera, H. W.; Pearce, R. *Can. J. Chem.* **1971**, *49*, 1618. (b) Brook, A. G.; Pearce, R.; Pierce, J. B.; *Ibid.* **1971**, *49* 1622. (c) Brook, A. G.; Pierce, J. B., Duff, J. M. *Ibid.* **1975**, *53*, 2874. (d) Brook, A. G.; Duff, J. M. *J. Am. Chem. Soc.* **1969**, *91*, 2118. (e) Brook, A. G.; Dillon, P. J.; Pearce, R. *Can. J. Chem.* **1971**, *49*, 133. (f) Porter, N. A.; Iloff, P. M., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 6200. (g) Brook, A. G.; Duff, J. M. *Can. J. Chem.* **1973**, *51*, 352. (h) Watanabe, H.; Kogure, T.; Nagai, Y. *J. Organomet. Chem.* **1972**, *43*, 285. (i) Watanabe, H.; Ohsawa, N.; Sawai, M.; Kukasawa, Y.; Matsumoto, H.; Nagai, Y. *Ibid.* **1975**, *93*, 1973. (j) Hassner, A.; Soderquist, J. A. *Tetrahedron Lett.* **1980**, 429.

[4] Dalton, J. C.; Evitt, E. R.; Wu, M. M. S., unpublished results.

[5] Only one of the two possible *cis*-cyclopropanes is observed, the exact stereochemistry of which has not yet been determined. No cis–trans isomerization of the maleate occurs.

[6] Bourque, R. A.; Davis, P. D.; Dalton, J. C. *J. Am. Chem. Soc.* **1981**, preceding paper in this issue.

[7] The inability of 2-propanol to quench cyclopropane formation does not rigorously rule out the possibility that siloxycarbene generated from the acylsilane S_1 state reacts with F to yield cyclopropane. (Such a mechanism would require that siloxycarbene generated from acylsilane T_1 state react with 2-propanol but not F, while siloxycarbene generated from the S_1 state reacts with F but not 2-propanol). The observation that F strongly quenches fluorescence of **4**, however, coupled with the fact that the quantum yield for non-acylsilane triplet-derived cyclopropane formation continually increases with increasing F concentration clearly indicates that the non-triplet-derived cyclopropane is coming from reaction of the acylsilane S_1 state with F. The only way significant amounts of cyclopropane could be formed via olefin reaction with siloxycarbene generated from S_1 would be if such a carbene were in equilibrium with the acylsilane S_1 state. This seems an unlikely possibility.

[8] (a) Murov, S. L. "Handbook of Photochemistry"; Marcel Dekker: New York, 1973; p 3. (b) From phosphorescence spectrum: Dalton, J. C.; Evitt, E. R., unpublished results. (c) Hammond, G. S., et al. *J. Am. Chem. Soc.* **1964**, *86*, 3197. (d) Turro, N. J. "Modern Molecular Photochemistry", Benjamin/Cummings: Menlo Park, CA, 1978; p 353.