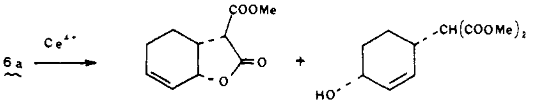
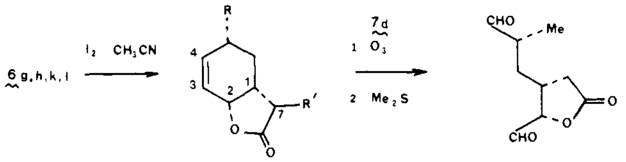
(**5**), both important macrolide antibiotics.[5] Our preliminary results are reported in this communication.

The diene complexes **1** and **2** reacted with $NaCH(CO_2Me)_2$, $NaCH(SO_2Ph)CO_2Me$, and $NaCH(COMe)CO_2Me$ in THF at 20 °C to give π-allyl complexes **6a–f** in high yield (75–95% isolated, pure compounds).[6] Attempted direct demetalation of diester **6a** ($Ce(NO_3)_6(NH_3)_2$, wet acetone, NaOAc)[7] gave a mixture of lactone **7a** (36% isolated) and hydroxy diester **8** (24% isolated). This method is therefore unsuitable for an approach to macrolide subunits. We envisioned a solution to the decomplexation problem by recognizing a possible analogy between the π-allyl–$Mo(CO)_2Cp$ unit and uncomplexed olefins. Thus, both types of molecule might show similar behavior toward electrophilic reagents, and on this basis we anticipated that iodolactonization of appropriate π-allyl–$Mo(CO)_2Cp$ derivatives might be accomplished. Accordingly, the diester complexes **6a** and **6d** were converted to the half acids **6g** and **6h** (KOH, MeOH, H_2O, THF, 20 °C, 10 h, 98% yield), and the phenylsulfonyl ester complexes **6b** and **6e** were converted to monoesters **6i** and **6j** (6% Na, Hg amalgam, Na_2HPO_4, MeOH, THF)[8] and thence to monoacids **6k** and **6l** (KOH, MeOH, THF, 20 °C, 5 h, 68% overall yield). Treatment of **6g** with *excess* iodine (4 equiv of I_2, CH_3CN, 20 °C) led to a rapid change in its IR spectrum: the $Mo(CO)_2$ bands at 1805 and 1927 cm^{-1} due to **6g** were replaced by two new bands at 2050 and 2082 cm^{-1}, their higher frequency suggesting the formation of a cationic π-allyl–$Mo(CO)_2ICp$ series. These new peaks slowly disappeared, with concomitant appearance of a γ-lactone absorption at 1780 cm^{-1}. On completion of the reaction, as judged from IR spectroscopy (ca. 30 min), aqueous workup and ether extraction afforded the lactone **7a**, pure according to TLC (90–95% yield). Simiarly, the acids **6h**, **6k** and **6l** were converted to lactones **7b–d** in very high yield. Ozonoloysis of **7d** (O_3, CH_2Cl_2, MeOH, −78 °C; Me_2S workup) afforded the dialdehyde **9**, which now has stereochemistry corresponding to C(5), C(6), and C(8) of tylosin and magnamycin B.



7a

8



7a, R = H; R' = α-CO_2Me
b, R = Me; R' = β-CO_2Me
c, R = R' = H
d, R = Me; R' = H

9

Thus, cyclohexadiene–$Mo(CO)_2Cp$ cations may be used for controlled functionalization of the six-membered ring, and the metal can be removed efficiently by using a novel iodolactonization/demetalation procedure to give potentially useful organic intermediates. Further aspects of this chemistry are currently under investigation in our laboratory.[9]

Acknowledgment. We are grateful to the National Institutes of Health for their financial support (GM-30757 and RR-07113-16) and the National Science Foundation for a grant toward the purchase of the Varian XL200 NMR spectrometer used in this research (CHE 80-24633).

---

(5) For some recent synthetic approaches to these macrolides, see the following references. Tylosin: Nicolaou, K. C.; Pavia, M. R.; Seitz, S. P.; *J. Am. Chem. Soc.* **1982**, *104*, 2027, 2030. Masamune, S.; Lu, L. D.-L.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *Ibid.* **1982**, *104*, 5523. Grieco, P. A.; Inanaga, J.; Lin, N.-H.; Yanami, T. *Ibid.* **1982**, *104*, 5781. Evans, D. A.; Bartroli, J.; Godel, T. *Tetrahedron Lett.* **1982**, *23*, 4577. Magnamycin B.: Tatsuta, K.; Amemiya, Y.; Maniwa, S.; Kinoshita, M. *Ibid.* **1980**, *21*, 2837.

(6) All compounds were obtained as racemic mixtures and were fully characterized by IR and 200-MHz ^1H NMR spectroscopy, high resolution mass spectrometry, and/or combustion analysis, exemplified by the following data for **6j**. Further details will be published in a full paper describing this work, as will the details of X-ray structure determination showing that addition of enolate nucleophiles occurs trans to the $Mo(CO)_2Cp$ group. **6j**: IR ν_{max} (CCl_4) 1945, 1870, 1740 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.29 (5 H, s, C_5H_5), 4.17 (1 H, t, J = 7.0 Hz, 2-H), 3.69 (3 H, s, CO_2Me), 3.75–3.5 (2 H, m, obscured, 1-H, 3-H), 2.55 (2 H, d, J = 6.8 Hz, CH_2CO_2Me), 2.3 (1 H, m, 4-H), 1.9 (1 H, m, 6-H), 1.22 (3 H, d, J = 7.2 Hz, Me), 0.85 (1 H, dm, J_{gem} = 14.5 Hz, *endo* 5-H), 0.65 (1 H, d, J_{gem} = 14.5 Hz, exo 5-H). The pattern observed for endo 5-H and exo 5-H is consistent with structure and stereochemistry **6j**. The absence of large coupling constants between exo 5-H and 4-H or 6-H is particularly diagnostic of the cis relationship between R and R' by comparison with the spectral data given by Faller[4] for complex **3**.

(7) We have previously used this method successfully with dienyl–$Mn(CO)_3$ complexes. Details are given in: Pearson, A. J.; Richards, I. C.; Bruhn, P. R. *Tetrahedron Lett.* **1984**, *25*, 387.

(8) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477.

(9) This mild decomplexation method appears to be general. Similar treatment of ester complexes related to **6a** leads to the formation of substituted iodocyclohexenes, and these aspects will be discussed in a full paper.

Observation of Cis and Trans Oxaphosphetanes in the Wittig Reaction by High-Field ^{31}P NMR Spectroscopy

Allen B. Reitz, Martin S. Mutter, and Bruce E. Maryanoff*

Chemical Research Department, McNeil Pharmaceutical
Spring House, Pennsylvania 19477

Received December 9, 1983

Vedejs and co-workers, in pioneering work on the Wittig olefination reaction, established oxaphosphetanes (e.g., **1** and **2**; see Scheme I) as key intermediates by low-temperature ^{31}P NMR spectroscopy (at 40.5 MHz), observing them as narrow multiplets (partial proton decoupling) between −55 and −75 ppm.[1] However, resolved ^{31}P NMR resonances for cis and trans oxaphosphetanes have generally not been observed,[1,2] thereby precluding direct quantitation and application of such data to mechanistic analyses.[3]

In connection with our research on Wittig reactions of carboxy and oxido ylides,[4] we initiated ^{31}P NMR studies to probe the effect of anionic groups on stereochemistry. Since experiments conducted with such ylides on a Bruker AM-360 instrument at 145.8 MHz (broad-band proton decoupling) revealed pairs of singlets between −55 and −65 ppm, attributable to diastereomeric oxaphosphetanes, we reexamined Wittig reactions involving simple alkylidene ylides. Salient features of our work include (1) the first observation of cis and trans oxaphosphetanes in the reaction of nonstabilized phosphorus ylides with aldehydes, (2) direct quantitation of the diastereomeric pairs by electronic integration, (3) assignment of the peaks via chemical arguments, and (4) demonstration of noncorrespondence between the ratios of cis/trans oxaphosphetanes

---

(1) (a) Vedejs, E.; Meier, G. P.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1981**, *103*, 2823. (b) Vedejs, E.; Snoble, K. A. J. *Ibid.* **1973**, *95*, 5778.

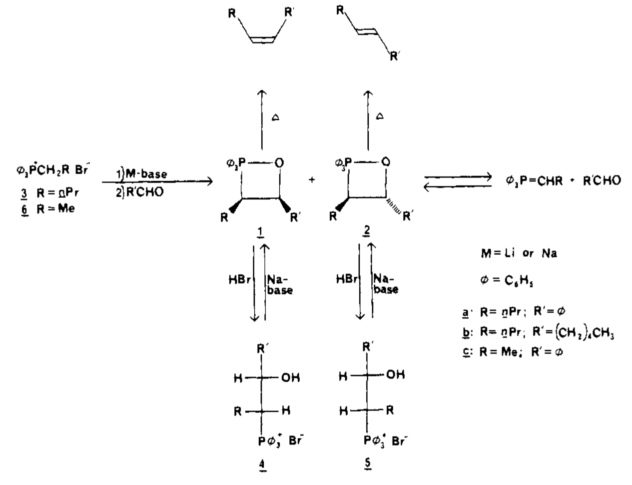
(2) (a) Schlosser, M.; Piskala, A.; Tarchini, C.; Tuong, H. B. *Chimia* **1975**, *29*, 341. (b) Bestmann, H. J. *Pure Appl. Chem.* **1979**, *51*, 515. (c) Vedejs, E.; Meier, G. P. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 56.

(3) Many mechanistic discussions of the Wittig reaction have been presented: (a) Schlosser, M. *Top. Stereochem.* **1970**, *5*, 1. (b) Schlosser, M.; Christman, K. F. *Justus Liebigs Ann. Chem.* **1967**, *708*, 1. (c) Gosney, I.; Rowley, A. G. In "Organophosphorus Reagents in Organic Synthesis"; Cadogan, J. I. G, Ed.; Academic Press: New York, 1979; pp 17–153. (d) Schlosser, M.; Schaub, B. *J. Am. Chem. Soc.* **1982**, *104*, 5821. (e) McEwen, W. E.; Cooney, J. V. *J. Org. Chem.* **1983**, *48*, 983. (f) References 1 and 2 b. (g) Bestmann, H. J. *Pure Appl. Chem.* **1980**, *52*, 771. Although much effort has been devoted to relating reaction stereochemistry with mechanism, through alkene *Z*/*E* ratios, the stereochemistry of reaction intermediates has generally been ignored.

(4) Maryanoff, B. E.; Reitz, A. B.; Duhl-Emswiler, B. A. *Tetrahedron Lett.* **1983**, *24*, 2477. Maryanoff, B. E.; Duhl-Emswiler, B. A. *Ibid.* **1981**, *22*, 4185.

0002-7863/84/1506-1873$01.50/0 © 1984 American Chemical Society

Scheme I



and Z/E alkenes in certain instances (with benzaldehyde and lithium cation).

Typical experiments were conducted with *n*-butyltriphenylphosphonium bromide (**3**) under argon. Thus, salt **3** in dry tetrahydrofuran (THF) was treated with 1.0 mol equiv of lithium hexamethyldisilazide (HMDS) at 22 °C to generate the ylide, evidenced by ^{31}P NMR (−30 °C) as a sharp singlet at 11.6 ppm. Addition of benzaldehyde (0.9 mol equiv) to an NMR sample at −78 °C produced a spectrum (−78 °C) featuring three major singlets: 12 (unreacted ylide), −61.4 (cis oxaphosphetane, **1a**), and −63.8 ppm (trans oxaphosphetane, **2a**); the two baseline-separated, upfield peaks integrated in a ratio of 3.8:1, respectively. On warming to −30 °C, the oxaphosphetane resonances became extremely sharp (cis/trans = 3.8:1), the ylide peak disappeared, and a new singlet arose at 28.0 ppm due to the formation of triphenylphosphine oxide (actually as a LiBr complex, confirmed independently). The course of the decomposition of oxaphosphetanes was monitored with time at −25 °C with integration of the resonances at 28.0, −61.4, and −63.8 ppm. The disappearance of oxaphosphetanes (**1a** + **2a**) and appearance of triphenylphosphine oxide occurred in a monotonic relationship, while the oxaphosphetane isomer ratio gradually changed, becoming enriched in the trans oxaphosphetane with time. As the conversion to phosphine oxide neared completion, the oxaphosphetane ratio became ca. 1:1. More significantly, the final alkene Z/E ratio of 1.5:1 did not reflect the original 3.8:1 ratio of **1a** to **2a**, probably because of the conversion of cis to trans oxaphosphetane during the decomposition process.[5] Several repetitions of this reaction gave related results; initial oxaphosphetane cis/trans ratio varied in the range of 6.0–3.0:1 and differed from ratios (ca. 1:1) near the reaction end point.

In an analogous fashion, the ylide from **3** and LiHMDS was treated in an NMR tube at −78 °C with hexanal. The ^{31}P[^{1}H] NMR spectrum at −30 °C exhibited two singlets at −59.7 and −64.3 ppm in a ratio of 5.8:1 (cis/trans, **1b**/**2b**). Again, the decomposition was monitored with time at −25 °C, whereupon a new resonance emerged for the triphenylphosphine oxide–LiBr complex as the oxaphosphetanes vanished. The ratio of **1b** to **2b** changed over the reaction course, becoming nearly 1:1 at the reaction endpoint, but in this instance the final alkene Z/E ratio of 5.8:1 corresponded to the initial oxaphosphetane ratio.[6]

Three important results are evident from these experiments. Cis and trans oxaphosphetanes disappear at different rates, the cis reacting faster than the trans in these examples. Second, oxaphosphetanes derived from benzaldehyde (aromatic aldehyde), but not hexanal (aliphatic aldehyde), undergo some form of equilibration at a rate competitive with the rate of decomposition, possibly through reversible interconversion of oxaphosphetanes and starting materials.[7] Third, although it has been recognized that aromatic aldehydes furnish diminished alkene Z/E ratios compared to aliphatic aldehydes,[3a–c] this may not be caused by a difference in the ylide–aldehyde condensation step; rather it appears to be caused by oxaphosphetane interconversion in the case of aromatic aldehydes (i.e., some degree of thermodynamic control).

Phosphonium salt **3** was also reacted with NaHMDS in THF at 22 °C and treated with benzaldehyde at −78 °C. The ^{31}P[^{1}H] NMR spectrum at −20 °C displayed only one sharp singlet in the upfield region (at −61.9 ppm) for cis oxaphosphetane **1a**, a singlet at 11.8 ppm for the ylide, and a minor singlet at 23.2 ppm for triphenylphosphine oxide. Workup of this reaction gave a 96:4 Z/E ratio of β-propylstyrenes, which reflects little oxaphosphetane equilibration. Since "salt-free" ylides demonstrate high Z selectivity,[3b,8] this experiment provided us with preliminary peak assignments.

To complete this investigation, we prepared **1a** and **2a** by deprotonation of the corresponding erythro and threo β-hydroxyphosphonium salts[9] (**4a** and **5a**; see Scheme I). A mixture of **4a** and **5a** was obtained as a white solid (75% yield) by sequential treatment of **3**, at −78 °C, with *n*-butyllithium (1 mol equiv; 1.6 M in hexane), benzaldehyde, and anhydrous HBr. A ^{31}P[^{1}H] NMR spectrum ($CDCl_3$) showed two singlets at 25.4 and 23.1 ppm in a ratio of 2.6:1 for the erythro (**4a**) and threo (**5a**) hydroxyphosphonium salts. In a similar reaction sequence with LiHMDS, the erythro/threo ratio was found to mirror the cis/trans oxaphosphetane ratio measured by low-temperature ^{31}P[^{1}H] NMR. Fractional crystallization of the 2.6:1 mixture afforded **4a**, which exhibited one singlet at 25.4 ppm (^{31}P[^{1}H] NMR).[10] A Schlosser trans-selective Wittig reaction,[11] in which an extra equivalent of *n*-butyllithium was added to the oxaphosphetane mixture at low temperature before the HBr addition, gave crystalline **5a** (60% yield), showing one singlet at 23.1 ppm.[10] The pure samples of **4a** and **5a** were deprotonated with NaHMDS in THF at −40 °C to generate the respective oxaphosphetanes; each ^{31}P NMR spectrum demonstrated single peaks, at −62.2 (**4a**) and −64.4 ppm (**5a**). The corresponding alkene products formed in Z/E ratios of 97:3 (**4a**) and 2:98 (**5a**), indicative of little or no equilibration of intermediates prior to decomposition (Na as the cation). These studies with **4a** and **5a**, besides confirming the oxaphosphetane peaks in the ^{31}P NMR spectra of the Wittig reactions, strongly support our peak assignments for the oxaphosphetane diastereomers.[12]

Since Vedejs[1] and Schlosser[2a,3b,d] devoted attention to ethylidenetriphenylphosphorane, as opposed to butylidenetriphenylphosphorane, we examined this system for comparison. Analogous reaction of ethyltriphenylphosphonium bromide (**6**) with LiHMDS and benzaldehyde gave a 145.8-MHz ^{31}P NMR spectrum with two barely resolved singlets at −61.2 and −61.6 ppm, in a ratio of ca. 4:1; workup provided β-methylstyrenes in a Z/E ratio of 2:1, again illustrating equilibration of intermediates. The proximity of these oxaphosphetane resonances makes this a poor system for quantitative studies; thus, we refrained from experimenting with **4c** and **5c**. In should be noted, however, that other oxaphosphetane diastereomers, from the reaction of benzaldehyde with the following ylides, are represented by well-separated pairs of ^{31}P NMR resonances in the region between −58 and −65 ppm: $Ph_3P{=}CH(CH_2)_2O^-$ (Li^+), $Ph_3P{=}CH(CH_2)_4O^-$(Li^+), and

---

[5] Alkene Z/E ratios were determined by GLC (SE-30/Chromosorb Q column); identification of alkenes was accomplished by GLC/MS and ^{1}H NMR.

[6] The alkenes were analyzed[5] in this case as a mixture of epoxides (prepared with MCPBA).

[7] For a discussion of reversibility, see ref 1a and papers cited therein.

[8] Bestmann, H. J.; Stransky, W.; Vostrowsky, O. *Chem. Ber.* **1976**, *109*, 1694.

[9] The hydroxyphosphonium salts were obtained in a manner analogous to that of Schlosser,[3b] except that HBr was added at −78 °C instead of 0 °C to avoid oxaphosphetane decomposition along with alteration of the stereochemistry.

[10] Salts **4a** and **5a** were characterized by 360-MHz ^{1}H NMR and microanalytical data, which are presented in the supplementary material (along with melting point data).

[11] Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 650.

[12] Single-crystal X-ray analysis of **5a** (by Prof. R. A. Olofson) has verified the threo assignment. Details will be reported elsewhere.

$Ph_3P{=}CH(CH_2)_3COO^-$ (Li^+ or Na^+).[13] Such direct observation of individual oxaphosphetanes allows the stereochemistry of initial carbon–carbon bond formation to be unambiguously determined for the first time.

We are currently using high-field ^{31}P, ^1H, and ^{13}C NMR to investigate reaction kinetics and thereby obtain a more complete picture of the Wittig reaction process.

Supplementary Material Available: Melting points, 360-MHz ^1H NMR data, and elemental analyses for **4a** and **5a** (1 page). Ordering information is given on any current masthead page.

---

(13) Oxaphosphetane diastereomers prepared from ylides bearing anionic groups appear at roughly the same chemical shifts as those prepared from **3**. Results with these ylides will be described elsewhere.

Chemiluminescence in the Infrared Photochemistry of Oxetanes: The Formal Reverse of Ketone Photocycloaddition

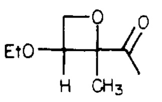
William E. Farneth*† and Douglas G. Johnson

Department of Chemistry, University of Minnesota
Minneapolis, Minnesota 55455

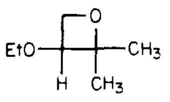
Received August 24, 1983

Multiphoton excitation using infrared lasers (IRMPE) is an excellent method for making ensembles of highly vibrationally excited ground-state molecules.[1] At low enough pressures and with sufficiently intense lasers, these "vibrationally hot" molecules may undergo chemical reaction. In general, the chemistry resembles thermal chemistry and the lowest energy pathway predominates. In certain cases, however, reaction channels that are not accessible under normal thermal conditions compete.[2] In this paper we report the observation of an IRMPE-induced decomposition leading to a diabatic, chemiluminescent channel that occurs in competition with the normal, adiabatic ground-state thermal reaction. The reaction we have studied is the fragmentation of oxetanes to ketones and olefins. The diabatic reaction produces electronically excited ketone. It represents the formal reverse of the well-known photochemical cycloaddition of ketones to olefins, the Paterno–Buchi reaction (Scheme I).[3] This constitutes a rare example of a diabatic organic reaction in which it is possible to access electronic surface crossing regions starting from either side of the reaction coordinate.[4]

Oxetanes **1** and **2** have been prepared by the photochemical cycloaddition of biacetyl[5a] and acetone,[5b] respectively, with ethyl vinyl ether (EVE).



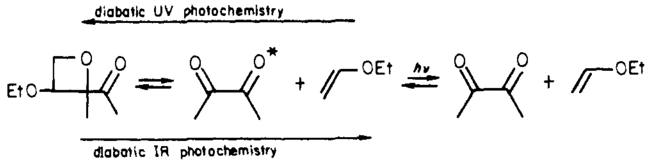
1



2

As has been previously noted, cycloaddition occurs regioselectively,[3] and with biacetyl, with relatively high stereoselectivity as well.[5a] **1** is formed as a 9:1 mixture of diastereomers. The diastereomers have not been separated, but the mixture has been purified by preparative gas chromatography for use in the IR photochemistry.

Scheme I



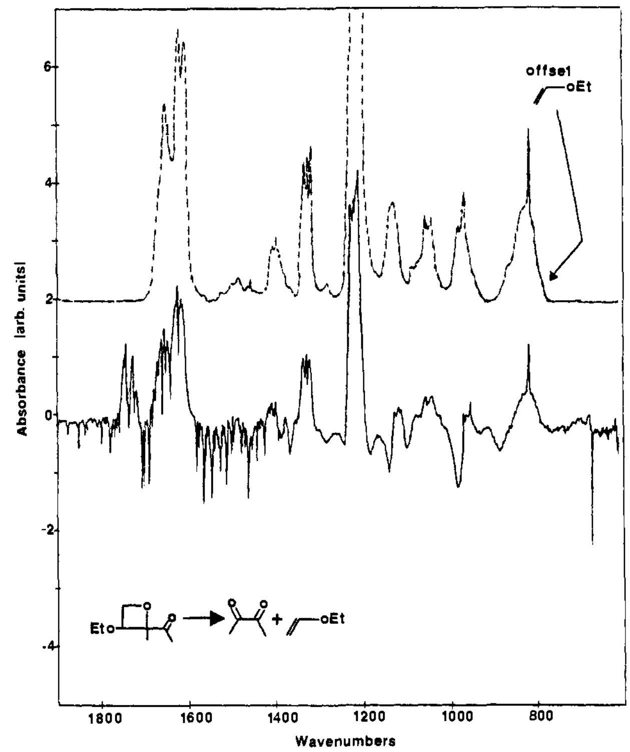


Figure 1. FTIR difference spectrum (photolysis mixture – starting material) after 600 pulses at ~2 J/cm². The dotted offset spectrum is ethyl vinyl ether vapor taken under similar conditions.

1 and **2** were irradiated in the gas phase with the collimated beam of a grating-tuned CO_2 TEA laser. Typical reaction conditions employed 0.1 torr of oxetane and 1.0 J/cm² fluence with a beam diameter of 6 mm, constant through the cell at a frequency of 969.15 cm^{-1} [R(10) 001–100]. Progress of the reaction was conveniently followed by continuously monitoring the pressure in the cell. Up to 25% conversion, the pressure data give a good fit to a first-order rate constant calculated according to the stoichiometry of Scheme I:

$$-k = \frac{1}{t} \ln \frac{2P_0 - P_t}{P_0}$$

For **1**, products have been analyzed by GC and IR.[6] Gas chromatography shows no significant products (<2%) other than biacetyl and ethyl vinyl ether, which are present in approximately equal concentration. Infrared spectroscopy clearly shows the growth of absorption features assigned to the ketone and olefin. Figure 1 is the FTIR difference spectrum of a sample of **1** irradiated for 600 pulses, from which the starting oxetane spectrum has been subtracted. It is clear from Figure 1 that all the major features in this spectrum can be assigned to ethyl vinyl ether (spectrum superimposed). The carbonyl bands of biacetyl at 1725 and 1735 cm^{-1} are also evident.[7] The rate of IR photodecomposition of oxetanes appears to respond as would be expected from previous work to changes in fluence, frequency, and bath gas pressure.[8]

---

† Central Research & Development Department, E. I. du Pont de Nemours & Co., Experimental Station, Wilmington, DE 19898.

(1) Danen, W. C.; Jang, J. C. In "Laser-Induced Chemical Processes"; Steinfeld, J. I., Ed.; Plenum Press: New York, 1981; and references therein.

(2) Farneth, W. E.; Thomsen, M. W. *J. Am. Chem. Soc.* **1983**, *105*, 1843.

(3) Jones, G., II *Org. Photochem.* **1981**, *5*, 227.

(4) Turro, N. J.; Chow, M.; Rigaudy, J. *J. Am. Chem. Soc.* **1979**, *101*, 1300.

(5) (a) Ryang, J.; Shima, K.; Sakuri, J. *J. Org. Chem.* **1973**, *38*, 2860. (b) Schroeter, S. H.; Orlando, C. M., Jr. *Ibid.* **1969**, *34*, 1181.

(6) Photolysis mixtures were directly injected into a gas chromatograph via a gas injection port. Columns of either 8% UCON-LB550X or 10% QF-1 (1/8 in. × 10 ft., Chromosorb W solid support) were used.

(7) Gas phase FTIR spectrum of biacetyl was taken under similar conditions.

(8) Farneth, W. E.; Thomsen, M. W.; Schultz, N. L.; Davies, M. A. *J. Am. Chem. Soc.* **1981**, *103*, 4001.

0002-7863/84/1506-1875$01.50/0