ether **12** and subsequently oxidatively demethylated[8b] with silver oxide and hydrolyzed to give the desired tetracyclic trione **4** in 77% yield. This oxidation could not be successfully scaled up, and as an alternative we found that the dimethyl ether **13b** could be cleanly demethylated selectively at the 6-position with 1:1 HBr/HOAc to give in larger scales the trione **4**, which had ^{1}H NMR, IR, and mass spectra identical with those of an authentic sample. That the 6-methoxyl in **13b** is selectively cleaved can also be established by the same conversion for **13c** prepared from the ethoxycarbene complex **1c**. The synthesis of the tetracyclic trione **4** was achieved in nine steps from commercially available starting materials in 8% overall yield and is thus comparable to the other syntheses of this intermediate.[8]

The synthesis of the intermediate **4** not only represents a formal synthesis of daunomycinone **6a**[9] but also demonstrates that the strategy of utilizing the benzannulation of cyclohexenyl chromium carbene complexes as outlined in Scheme II is a viable approach to anthracycline synthesis. Moreover, it can be anticipated to be a powerful approach since fully functionalized aglycones (i.e., **6a**) could be obtained directly from the corresponding cyclization of more highly functionalized carbene complexes and since it could at the same time provide for a convergent synthesis for both the 11-oxy and 11-deoxy anthracyclines due to the fact that the benzannulated product **9** has the oxygens in the incipient 6- and 11-positions differentially protected.

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Infrared Spectrum and Photochemistry of Methoxychlorocarbene

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Oxygen-substituted carbenes have drawn considerable attention.[2] Interaction between the carbene unoccupied p orbital and the adjacent oxygen lone pair is thought to stabilize the singlet state relative to the triplet[3] and to increase the nucleophilicity in oxycarbenes.[4] The simplest member of this family, hydroxymethylene, has been suggested as an intermediate in formaldehyde photochemistry, although it has eluded spectroscopic detection.[5] Alkoxycarbenes have similarly been implicated as photoproducts of cyclobutanones and certain other cyclic ketones.[6] Methoxychlorocarbene (**1**) was proposed by Hine and co-workers in 1953[7] to be an intermediate in the alkaline methanolysis of chloroform. More recently, the groups of Moss[8] and Stevens[9] have investigated the reactions of **1** generated by thermolysis of 3-chloro-3-methoxydiazirine (**2**). Two aspects of the chemistry of **1** are of particular note. First, methoxychlorocarbene (**1**) is the premier example of an ambiphilic singlet carbene.[4,8,9] The substituent effects produce a species exhibiting both electrophilic and nucleophilic proclivities. Second, **1** does not thermally rearrange to acetyl chloride, but rather generates methyl chloride and CO if untrapped.[9] Although the mechanism of this reaction is uncertain, carbocations have been suggested as intermediates in the decomposition of other alkoxychlorocarbenes.[10] This is in striking contrast to non-halogen-substituted oxycarbenes, which generally undergo alkyl migration to give the corresponding carbonyl compounds,[6,11] albeit likely via biradicals.

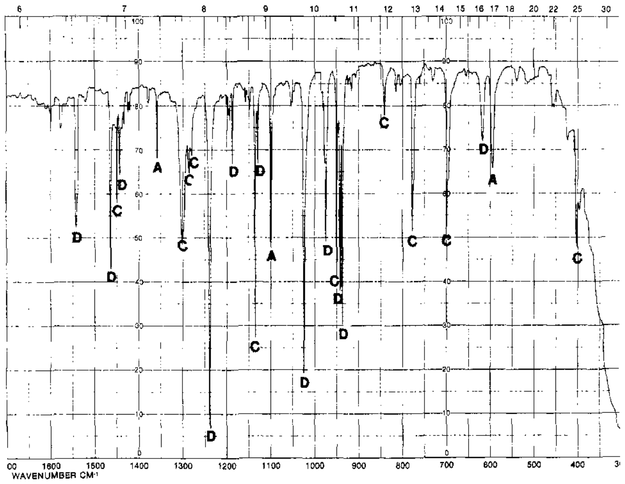
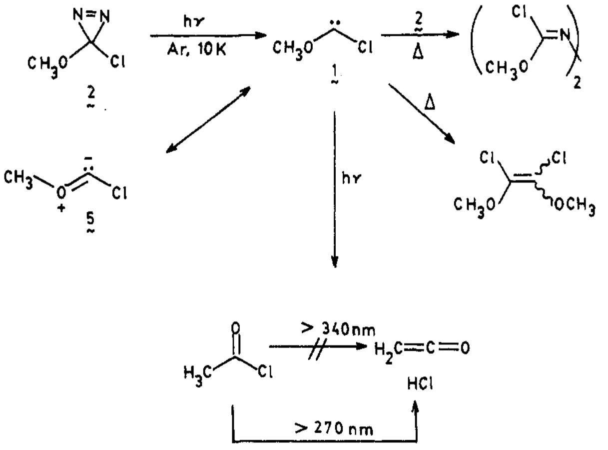


Figure 1. Infrared spectrum obtained on irradiation (λ >340 nm) of argon matrix isolated (1:700; 10 K) 3-chloro-3-methoxydiazirine (**2**). Bands marked C are assigned to methoxychlorocarbene (**1**), those marked D are due to **2**, and those marked A are from acetyl chloride.

Although a number of carbenes have been characterized by IR, ESR, and UV,[2] no oxycarbenes have been directly observed. We now wish to report the IR spectrum of methoxychlorocarbene (**1**), its novel photochemistry, and information concerning its molecular structure.

Irradiation (λ >340 nm) of argon matrix isolated 3-chloro-3-methoxydiazirine (**2**)[9,12] at 10 K produces a new species with major IR absorptions at 2963, 1449, 1300, 1286, 1280, 1135, 950, 842, 777, 698, and 402 cm^{-1} (Figure 1). The product is photolabile at these wavelengths and is converted to acetyl chloride, ketene, and HCl on continued irradiation.[13] This photoreactivity limits



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[12] Matrix samples were prepared in dilutions of 1:600 to 1:1000 in argon and deposited from the gas phase onto a 2.54-cm CsI window cooled by an Air Products, Inc., Displex 202 refrigerator. Irradiations were performed with a Varian EIMAC 300-W high-pressure Xe arc lamp through a water filter and appropriate cutoff filters. Infrared spectra were recorded on a Beckman 4250 spectrometer.

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the extent to which this intermediate can be built up. No diazo intermediate (1900–2300 cm^{-1}) was observed, nor were chlorooxirane[13] or methyl chloride formed.[13] Ketene and HCl do not arise from secondary photolysis of acetyl chloride. Independent experiments showed acetyl chloride to be photochemically stable at these wavelengths (λ >340 nm), although higher energy irradiation (λ >270 nm) cleanly produces ketene and HCl in an argon matrix.[14]

The identity of **1** as the initial photoproduct was confirmed by bimolecular reaction. Irradiation of a 3-methylpentane glass of **2** at 10 K produced the same IR absorptions as observed in argon. Warming the matrix to 80 K caused the disappearance of the photoproduct IR bands with concurrent generation of a mixture of azine **3** and dimer **4**.[13] These products are sensibly derived from reaction of carbene **1** with starting diazirine or with another carbene molecule, respectively.

The IR spectrum of **1** provides significant insight into its electronic structure. Of particular concern is the relative importance of π-bonding as indicated in **5**. A logical comparison may be made between the IR spectrum of **1** and that of chloromethyl methyl ether, for which a complete vibrational analysis has been reported.[15] Chloromethyl methyl ether shows a C–O–C antisymmetric stretch at 1120 cm^{-1} and has only CH_2 deformations in the region from 1200 to 1400 cm^{-1}.[15] In contrast, a major band in the IR spectrum of **1** appears at 1300 cm^{-1}. Deuterium labeling shows that this absorption is not due to a methyl deformation. Irradiation of the trideuterio analogue of **2** in an argon matrix gives the trideuterio carbene, with IR absorptions at 2178, 1370 (weak), 1330, 1324, 1073, 1053, 926, 807, 755, 680, and 386 cm^{-1}. In particular, methyl absorptions in the 1450-cm^{-1} region are absent, but the ca. 1300-cm^{-1} band remains. We thus assign this absorption to the C–O–C antisymmetric stretch of the carbene.[16] The higher frequency compared to the corresponding stretch in $ClCH_2OCH_3$ indicates considerable C–O double-bond character. This conclusion is supported by ab initio calculations by Schaefer and co-workers, who predict the C–O stretch in hydroxymethylene to be 1381 cm^{-1}.[17,18]

In contrast to thermolysis results,[8,9] matrix isolated **1** rearranges photochemically to acetyl chloride. This transformation likely involves either a concerted 1,2-methyl migration or C–O bond cleavage to give a radical pair followed by recombination. More enigmatic is the conversion of **1** to ketene and HCl. Although it is a logical intermediate, acetyl chloride gives ketene at shorter wavelengths only. An appealing mechanism thus involves the adiabatic conversion[19] of electronically excited carbene to electronically excited acetyl chloride. The excited acetyl chloride subsequently cleaves to HCl and ketene. Simple-minded calculations indicate that the adiabatic conversion is energetically feasible. Rondan, Houk, and Moss[4] have calculated (4-31G) the energy for the isodesmic reaction, $:CH_2 + CH_3Cl + CH_3OCH_3 \rightarrow ClCOCH_3 + 2CH_4$, to be −60.3 kcal/mol. Using the known heats of formation for the other species[20] in this equation gives an estimated $\Delta H_f°$ of 2.9 kcal/mol for **1**. Our photochemical results indicate that the longest wavelength where rearrangement of the carbene takes place is 360 nm. Combining this energy, the heats of formation of acetyl chloride[20] and **1** and the UV spectrum of acetyl chloride[21] indicates that rearrangement of excited singlet **1** to excited singlet acetyl chloride is exothermic by ca. 30 kcal/mol. Although the topology of the relevant energy surface is not known, the reaction clearly fulfills at least the energetic requirements for an adiabatic photoreaction.[19] Since acetyl chloride does not fluoresce, this mechanism must remain tentative at this time. Further studies on the chemistry and structure of **1** are in progress.[22]

Acknowledgment. We thank the Camille and Henry Dreyfus Foundation for support of this work. The infrared spectrometer and lamp were purchased in part with funds from the National Science Foundation (CHE-81173180).

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(22) Although two conformations are possible for carbene **1**, we have no direct evidence for either isomer. It is interesting to note that the ca. 1330-cm^{-1} band in the trideuterio compound is split into two distinct absorptions, which may indicate two conformers.

A General Procedure for Assigning the ^{31}P Spectra of Nucleic Acids

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One of the more promising approaches to the investigation of the conformations and molecular dynamics of polynucleotides is the use of phosphorus-31 nuclear magnetic resonance (^{31}P NMR).[1-5] The full potential of ^{31}P NMR has not been utilized since there has been no unambiguous method for assigning the signals. Thus, the information present in the chemical shifts has not been fully exploited, nor have the molecular dynamics of distinct sites been well explored.

Unlike many other elements, phosphorus does not have a suitable isotope for the purpose of assigning NMR resonances. Thus, we were led to develop the use of ^{17}O directly bonded to the phosphorus of polynucleotides as a means of specifically and unobtrusively labeling particular sites. The introduction of ^{17}O induces an appreciable increase in the line width of the ^{31}P resonances of polynucleotides and hence presents an unambiguous assignment procedure that is also applicable to nucleic acid–protein complexes.

For the phosphorus nuclei of polynucleotides there are two main contributions to transverse relaxation: dipolar and chemical shift anisotropy.[1-5] The two pathways contribute about equally to the transverse relaxation of ^{31}P when the experiment is performed at 4.7 T.[1-5] The dipolar relaxation is due to the 5′, 5″, and 3′ protons of the polynucleotide, which are between 0.26 and 0.28 nm away from the phosphorus nucleus. When the phosphorus is directly bonded to ^{17}O two additional relaxation pathways come into play. Scalar relaxation of the second kind arises from rapid modulation of the ^{31}P–^{17}O scalar coupling due to the quadrupolar relaxation of the ^{17}O and is given by[6]

$$\frac{1}{T_{2SK}} = \frac{1}{3}S_Q(S_Q + 1)J^2\left(T_{1Q} + \frac{T_{2Q}}{1 + (\omega_P - \omega_Q)^2 T_{2Q}^{\,2}}\right) \qquad (1)$$

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