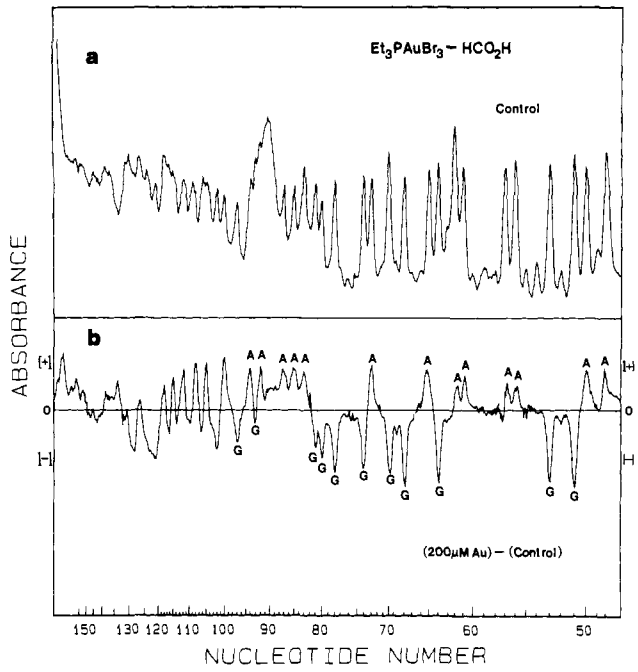

Figure 2. Microdensitometric scans of autoradiographic data involving HCO_2H/piperidine treatment of the restriction fragment in the presence and absence of **2** are shown. Absorbance scan of the control (a), no **2**, and the difference scan, 200 μM **2** − control (b).

inhibits formic acid induced cleavage at all of the guanine residues of the fragment. Since acid depurination initially involves protonation at the most basic site of the purine, in this case N-7,[9] gold binding to this site would inhibit protonation and thus the strand scission process. Figure 2 also shows that while cleavage at G is inhibited by **2**, the gold compound *enhances* cleavage at the adenine residues of the fragment. This phenomenon can be explained by gold binding to adenine and/or possibly thymine in such a manner which disrupts the Watson and Crick hydrogen bonding between A and T. Disruption of hydrogen bonding between these bases would expose adenine to facile protonation, ultimately resulting in a strand break in the polymer. A parallel can be found with the Au(III) complex $HAuCl_4$ which is believed to bind to all of the bases of DNA but shows an affinity for AT sites.[3d,10] This complex causes increased hyperchromicity upon binding to DNAs having a high (A + T) content, suggesting that base unpairing at the interaction site may be occurring.

The groups that are lost from **2** upon the binding of the complex to DNA are presently unknown. However, a single-crystal X-ray analysis of the compound revealed that the Au–Br bond *trans* to the phosphine ligand is longer (2.47 Å) than the remaining Au–Br bonds (2.41 Å) of the compound.[11] Thus, on the basis of the kinetic trans effect, the trans bromide should be the ligand which is most readily lost in the binding of **2** to DNA. However, a recent study[12] has shown that **2** reacts with deprotonated phthalimide (ptm) in nonaqueous media to yield as the major product the unexpected *cis* isomer, i.e., *cis*-$[AuBr_2(ptm)P(C_2H_5)_3]$. Ascertaining which ligands are lost from **2** and, if and to what extent the complex acts in a mono or bidentate fashion toward DNA will require further investigation.

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A Diazirine Precursor for a Dioxacarbene: Generation and Reactions of Methoxyphenoxycarbene

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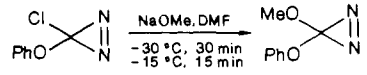
The archetypal nucleophilic carbene[2] dimethoxycarbene has been generated by pyrolyses of 7,7-dimethoxynorbornadienes[3] or hexamethoxycyclopropane[4] and by diisopropylethylamine deprotonation of the carbene's conjugate acid, dimethoxymethyl cation.[5] Much has thus been learned about the carbene's chemistry, but these generative methods require either elevated temperature or nonneutral conditions, precluding studies at low or ambient temperatures or in alkenic solvents, respectively. We now report the first instance of dioxacarbene generation from a diazirine precursor under mild and neutral conditions, as well as preliminary results of reactivity and theoretical studies that accord with anticipated nucleophilic properties.

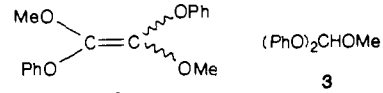
In analogy to other halodiazirine exchange reactions,[6] reaction of 3-bromo-3-methoxydiazirine[7] with methoxide should furnish 3,3-dimethoxydiazirine, an ideal precursor for dimethoxycarbene. Preliminary studies suggested that this exchange did proceed but that the dimethoxydiazirine was unstable under the generative conditions.[8] Accordingly, we targeted 3-methoxy-3-phenoxydiazirine (**1**) as a more accessible dioxacarbene precursor. 3-Chloro-3-phenoxydiazirine[9] was converted[6] to **1** by stirring with 5-fold excess of fresh NaOMe in dry DMF, eq 1.



(1)

1

Diazirine **1** was extracted with cold pentane from a crushed ice/water quench of the reaction mixture, dried ($CaCl_2$, SiO_2), filtered, and concentrated under vacuum at −30 °C. Yields of yellow **1** ranged from 60% to 90%; λ_{max} (pentane) 362 nm; IR (CCl_4) 1545 cm^{-1} (N=N);[7] ^1H NMR (δ_{CCl_4}) 3.50 (OMe), 7.06 (C_6H_5). Monitored by UV, **1** in pentane decayed thermally at 25 °C with first-order kinetics, presumably to methoxyphenoxycarbene (MeOCOPh); $k = 1.81 \times 10^{-4}$ s^{-1}, $\tau_{1/2} = 64$ min, $E_a \sim 20$ kcal/mol ($20 < T < 50$ °C). The decomposition products (90%) were the cis and trans MeOCOPh dimers **2** and diphenyl methyl orthoformate (**3**) in a 45:45:10 distribution.



2

3

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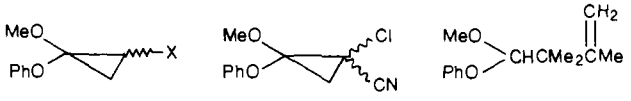
The dimers were isolated by crystallization from pentane (affording a dimer with mp 104–106 °C) and by chromatography on SiO_2 (oily second dimer). Their structures were established by NMR (δ_{CDCl_3} 3.56 and 3.71, OMe s) and appropriate C,H or exact mass analysis. Orthoformate **3** is most likely formed by phenolic capture of MeOCOPh, with the phenol produced by reaction of MeOCOPh with adventitious water.[10] The oily orthoformate was isolated by HPLC and characterized by NMR (δ_{CDCl_3} 3.57, OMe; 6.20, CH) and by GC/MS exact masses for its $(PhO)CH^+$ (10%) and $PhOCH^+OMe$ (100%) fragment ions.

Thermal decompositions (15 h, 25 °C) of diazirine **1** in acrylonitrile, methyl acrylate, α-chloroacrylonitrile, and tetramethylethylene led to products **4–7**. In the latter case, olefin **7**[11]



4, X = CN
5, X = COOMe
6
7

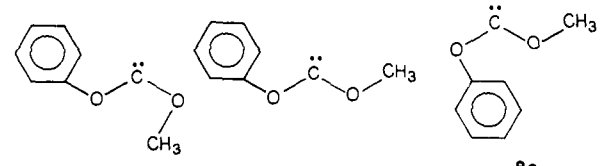
could result either from rearrangement of the anticipated cyclopropane or from an "ene" reaction between MeOCOPh and $Me_2C{=}CMe_2$. A similar product is formed in the analogous reaction of MeOCPh.[12]

Adducts **4–6** were formed in >90% yield (GC), purified by Kugelrohr distillation or chromatography (**5**), and characterized by appropriate NMR and exact mass spectra.[13] Isomer ratios were ca. 1.3:1 (**4**), 4:1 (**5**), and 2:1 (**6**), but syn/anti assignments have not been made.

The calculated[2] "carbene selectivity index" (m_{CXY}) of MeOCOPh is 2.11, only slightly lower than that calculated for $(MeO)_2C$ (2.22) and clearly in the region of the selectivity spectrum associated with nucleophilic carbenes.[2,14] Initial competition experiments for additions of thermally generated (25 °C) MeOCOPh to equimolar binary mixtures of $Me_2C{=}CMe_2$, $CH_2{=}CHCN$, or $CH_2{=}CClCN$ give a substrate reactivity order of 1:28:870, respectively, in accord with nucleophilic selectivity by MeOCOPh.

Ab initio restricted Hartree–Fock calculations were carried out on MeOCOPh by using standard basis sets and methods available in the GAUSSIAN 82 series of programs.[15,16] The carbene's geometry, including all C–O bond lengths and angles,[17] was optimized with the minimal STO-3G basis set; energies were subsequently obtained from 4-31G calculations at the optimized geometries.[16,17] "Low-energy" conformers **8a–c** were revealed by the calculations; a fourth conformer, where the CH_3 group of **8c** adopts the position it holds in **8a**, lies >16 kcal/mol above **8a**.

With oxacarbenes, strong interaction between oxygen lone pair electrons and the (singlet) carbene vacant 2p orbital generates



	8a	**8b**	**8c**
ϵ_{LU}, eV	+3.35	+3.33	+4.29
ϵ_{HO}, eV	−10.49	−10.78	−10.64
E_{rel}, kcal/mol	0.00	+1.27	+2.18

significant $—^-C{=}O^+—$ double-bond character in the carbenic C–O bonds, with consequent restricted rotation and the existence of "isomeric" carbenes at low temperatures; this holds true for MeOCOPh too.[18,19]

We also obtain the orbital energies associated with the filled carbenic σ orbitals (HOMO) and vacant p orbitals (LUMO) of **8a–c** (see above). These are quite similar to the calculated orbital energies of $(MeO)_2C$ (analogue of **8b**), $\epsilon_{LU} = +4.09$, $\epsilon_{HO} = -10.81$ eV,[20] so that the nucleophilicity of MeOCOPh is again understandable. More specifically, we estimated the differential orbital energies ($\epsilon_{CXY}{}^{LU} - \epsilon_{alkene}{}^{HO} = \Delta\epsilon_E$) and ($e_{alkene}{}^{LU} - \epsilon_{CXY}{}^{HO} = \Delta\epsilon_N$) associated with the electrophilic or nucleophilic modes of addition[2] of **8a–c** to tetramethylethylene and acrylonitrile. With MeOCOPh, nucleophilic addition to acrylonitrile is favored for conformers **8a–c** ($\Delta\epsilon_N < 11$ eV, $\Delta\epsilon_E > 14$ eV), and electrophilic addition of **8a** and **8b** to tetramethylethylene is not precluded ($\Delta\epsilon_E < 11.6$ eV, $\Delta\epsilon_N > 12.7$ eV), although steric hindrance to addition and the possibility of an ene reaction might account for the actual product, **7**.

The ease and simplicity of generation of MeOCOPh invite its further study as a representative nucleophilic carbene in reactions with a variety of sensitive substrates under extremely mild conditions. This work is in progress.

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(10) The yield of **3** increased with added water to the ultimate exclusion of **2**: MeOCOPh + H_2O → [MeOCH(OPh)OH] → PhOH + MeOOCH (not isolated). Decomposition of **1** in PhOH/MeCN gave mainly **3**.

(11) Kugelrohr distillation gave a 4.6:1:3.8 mixture of **2**, **3**, and **7**; δ_{CDCl_3}[7] 1.40 (s, 6 H, 2Me), 1.83 (s, 3 H, allylic Me), 3.53 (s, 3 H, OMe), 4.97 (d, $J \sim 4$ Hz, 2 H, $=CH_2$), 5.93 (s, 1 H, CH), 7.2 (m, aryl, with contributions from **2** and **3**). Purification of **7** is difficult, and we still regard the assignment of this structure as tentative. The mass spectrum even under chemical ionization, failed to show a molecular ion; *m/e* 177 was observed and attributed to the fragment ion $MeO(PhO)C{=}CMeC^+H_2$.

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(13) For example: δ_{CDCl_3}[4] 1.50–2.23 (m, 3 H, cyclopropyl CH), 3.50 (s, ratio 1:1.5, total 3 H, OMe of each isomer), 7.27 (m, 5 H, aryl). The isomers could be separated by HPLC or chromatography; definitive spectra were obtained on separated isomers at 400 MHz. MS, *m/e* calcd for $C_{11}H_{12}NO_2$ (M + 1, 100%) 190.0868; found 190.0879.

(14) (a) For example, the calculated m_{CXY} values associated with experimentally ambiphilic carbenes are considerably lower, including 1.74 (PhOCF), 1.59 (MeOCCl), and 1.49 (PhOCCl). (b) Cf.: Moss, R. A.; Kmiecik-Lawrynowicz, G.; Krogh-Jespersen, K. *J. Org. Chem.* **1986**, *51*, 2168 and references therein.

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(16) The procedures were strictly analogous to those employed in ref 14b.

(17) Complete numerical results will appear in our full paper.

(18) We calculated "transition-state" carbenes[17] for the conversions **8a** ⇌ **8b** and **8b** ⇌ **8c** at E_{rel} = 18.6 and 15.0 kcal/mol, respectively, above **8a**.

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Olefin Epoxidation by Manganese(IV) Porphyrins: Evidence for Two Reaction Pathways

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Synthetic metalloporphyrin complexes of iron,[1] manganese,[2] chromium,[3] and ruthenium[4] have been the focus of intense studies as models for the monooxygenase enzyme cytochrome P-450.

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