Table I. Total Intensities for Activators Used in Chemiluminescence Study

activator	ϕ_{fl}[a]	λ,[b] nm	ox. pot.,[c] V	corr tot intens[d]
acridine orange	1.0	515	0.72	1.05×10^8
9-dimethylamino[*b*]-benzophenazine	0.14	515	0.73	1.06×10^8
7-dimethylamino-2-methylphenazine	0.22	528	0.74	1.01×10^8
1,3-diphenyliso-benzofuran	0.96	475	0.79	3.40×10^7
rubrene	0.56	585	0.82	2.28×10^7
tetracene	0.21	486	0.87	1.59×10^7
DPET	0.66	583	0.97	8.08×10^6
perylene	0.84	475	1.06	3.20×10^6
DPEA	0.96	490	1.16	9.25×10^5
DPA	0.85	420	1.20	3.77×10^5

[a] Determined at 98 °C in deoxygenated *p*-xylene. [b] Wavelength monitored to determine chemiluminescence intensity. [c] Determined by cyclic voltammetry relative to SCE in CH_3CN with tetrabutylammonium perchlorate as supporting electrolyte. [d] Corrected for fluorescence efficiency of the activator and the spectral response of the chemiluminometer.

the chemiluminescence is shown in Figure 6.

Quenching of Diketone Formation from 1 with Dimethylmaleic Anhydride. Solutions of endoperoxide **1** (1.5×10^{-3} M) and dimethylmaleic anhydride (3.0×10^{-3} to 1.5×10^{-2} M) and eicosane (internal standard for gas chromatographic analysis) in *p*-xylene were degassed by freeze–pump–thaw techniques and sealed in individual glass ampules. The ampules were heated at 112 °C for 12 h. The yield of diketone **3** was determined by gas chromatography (see above). The data are shown on Figure 3.

Isolation and Identification of 1,3-Diphenylisobenzofuran 6 from the Thermolysis of Peroxide 1. A solution of peroxide **1** (120 mg) in 1.0 mL of *p*-xylene was deoxygenated by purging with dry Argon in a Pyrex test tube fitted with a Teflon stopcock. The solution was heated at 112 °C for 65 min at which time the maximum amount of yellow color had developed. The components of the thermolysis solution were separated by preparative HPLC on silica gel eluting with hexane–0.1% CH_3CN. The fraction that absorbed strongly at 390 nm was collected and the solvent evaporated, leaving a yellow residue (2 mg). The mass and ^1H NMR spectra of this residue and its melting point correspond with those of authentic (Aldrich) 1,3-diphenylisobenzofuran.

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Registry No. 1, 25994-58-5; **2**, 17023-28-8; **3**, 1159-86-0; **5**, 66819-90-7; **7**, 66819-89-4; maleic anhydride, 108-31-6; dimethylmaleic anhydride, 766-39-2; acridine orange, 65-61-2; 9-dimethylamino[*b*]benzophenazine, 80294-18-4; 7-dimethylamino-2-methylphenazine, 4661-61-4; **6**, 5471-63-6; rubrene, 517-51-1; tetracene, 92-24-0; DPET, 18826-29-4; perylene, 198-55-0; DPEA, 10075-85-1; DPA, 1499-10-1.

Effects of Substituents and Generation Methods on Insertion–Addition Selectivities of "Arylcarbene" in Alcohol–Olefin Binary Mixtures. Intervention of Reaction of Diazo Compounds Masquerading as Carbenes

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Abstract: A Hammett study of the insertion–addition selectivity (k_i/k_a) and cyclopropanation stereoselectivity (k_c/k_t) of "arylcarbene" generated either photolytically or thermally in 2-propanol–ethyl vinyl ether binary mixtures showed that ρ values are highly sensitive to the generation method. Thus, plots of k_i/k_a and k_c/k_t vs. σ (σ^+) in the photolytic run gave ρ values of −0.96 ($r = -0.96$) and −0.15 ($r = -0.95$), respectively, whereas similar values are +1.4 ($r = 0.93$) and −1.1 ($r = -0.96$) in the thermal run. The results along with the effects of precursor, temperature, and sensitizer on the product distributions are interpreted as indicating that, while free carbene is involved in the photolytic run, the ground-state diazo compound is masquerading as carbene in its thermal reaction with the olefin.

In view of the many cases in which formal carbenic products have been obtained in the photolysis and thermolysis of diazo compounds, the intermediacy of free carbenes in these experiments has been widely accepted.[1] However, as Kirmse stated in his book,[1b] "the long-lasting fascination of the carbene concept for organic chemists appears to have emotional rather than empirical grounds". Conceivably, excited precursor molecules may act as carbenoid species, mimicking free carbene in their reactions. In fact, a recent product analysis[2] as well as spectroscopic[3] studies revealed that carbene-mimicking reactions of excited diazo compounds are involved in the photochemical processes of several α-diazocarbonyl compounds. For example, it has been shown that the photochemical Wolff rearrangement to form ketene takes place directly from the singlet excited state of the *s*-*Z* conformer whereas the excited state of the *s*-*E* conformer dissociates nitrogen to

(1) See for reviews: (a) Moss, R. A.; Jones, M., Eds. "Carbenes"; Wiley: New York, 1973, 1975; Vols. I, II. (b) Kirmse, W. "Carbene Chemistry", 2nd ed.; Academic Press: New York, 1971.

(2) (a) Tomioka, H.; Kitagawa, H.; Izawa, Y. *J. Org. Chem.* **1979**, *44*, 3072. (b) Tomioka, H.; Okuno, H.; Izawa, Y. *Ibid.* **1980**, *45*, 5278. (c) Tomioka, H.; Kondo, M.; Izawa, Y. *Ibid.* **1981**, *46*, 1090. (d) Tomioka, H.; Okuno, H.; Kondo, S.; Izawa, Y. *J. Am. Chem. Soc.* **1980**, *102*, 7123. (e) Kaplan, F.; Mitchell, M. L. *Tetrahedron Lett.* **1979**, 759.

(3) (a) Roth, H. D.; Manion, M. L. *J. Am. Chem. Soc.* **1976**, *98*, 3392. (b) Roth, H. D. *Acc. Chem. Res.* **1977**, *10*, 85.

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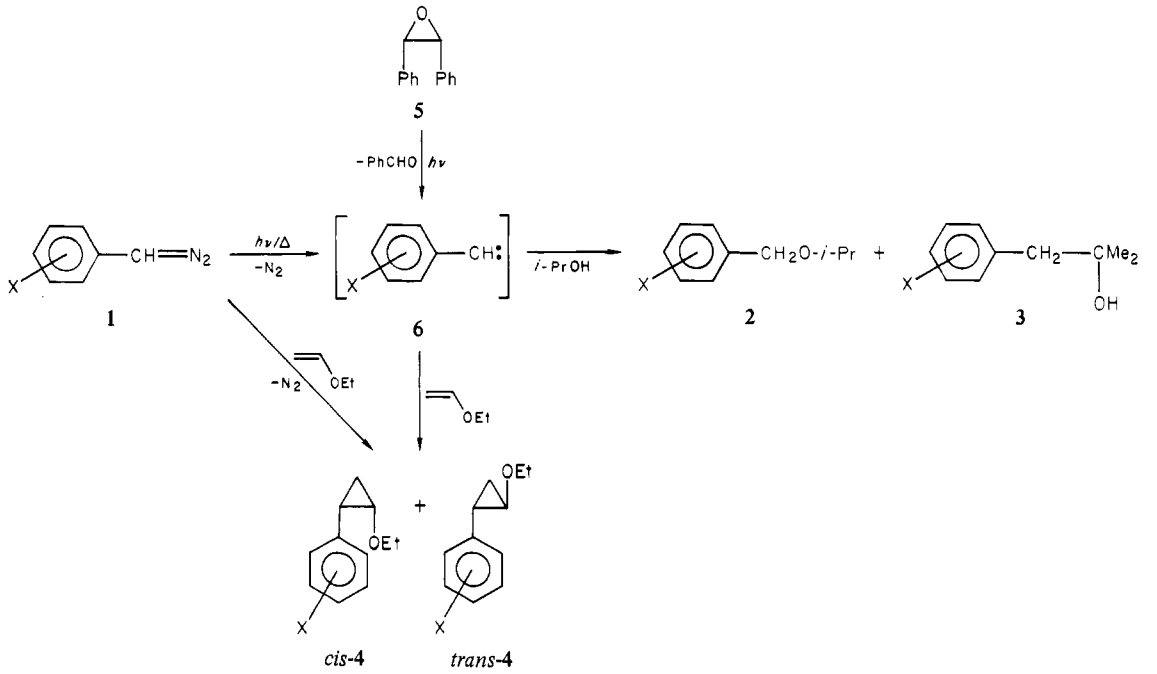
Scheme I



a, X = *p*-MeO; b, X = *p*-Me; c, X = H; d, X = *p*-Cl; e, X = *m*-MeO; f, X = *p*-Br; g, X = *m*-Cl

generate singlet carbene, which either undergoes characteristic carbene reactions or gives rise to ketene.[2b,c,3] Moreover, investigation of the photolysis of α-diazoamide has suggested[2a,b] that the excited singlet of the *s*-*Z* conformer undergoes H abstraction to give a formal carbenic intramolecular C–H insertion product, i.e., β-lactam, whereas that of the *s*-*E* conformer gives singlet carbene which undergoes another intramolecular C–H insertion to give γ-lactam. Although there are ample examples indicating that carbene reactivities have been highly dependent on the method of generation, they have been mainly explained in terms of the differences in multiplicities and energy contents of reacting carbene. Recently, it has been suggested[4] that excited singlet carbene could be responsible for much of the chemistry occurring on direct irradiation of alkyl diazo compounds and diazirines. The suggestion is made in order to explain the differences in reaction pattern of carbene generated photolytically (direct or sensitized) and thermally. In a continuing effort to determine whether precursors are involved in observed chemical reactions, we have examined the OH insertion–olefin addition selectivity of "arylcarbene" generated photolytically and thermally and wish to present kinetic data indicating that the ground-state diazo compound is masquerading as a carbene in its thermal reaction with olefin.

Results and Discussion

Irradiation of phenyldiazomethane (**1c**) in a binary mixture (1:1) of degassed 2-propanol–ethyl vinyl ether through a Pyrex filter at 20 °C gave 2-propyl benzyl ether (**2c**, 26.1%) and cyclopropanes (**4c**, 58.9%, cis/trans = 0.83) along with small amounts of C–H insertion product (**3c**), toluene, bibenzyl, and aldazine (Scheme I). Product ratios were found to be sensitive to the aryl substituents of **1**; electron-donating substituents favor ether formation (insertion), while electron-withdrawing substituents favor cyclopropanation (addition). Insertion (k_i)–addition (k_a) selectivities of arylcarbene were calculated by means of the well-established equation (**1**),[5] where P_i and P_a are the moles of

$$k_{rel} = \frac{k_i}{k_a} = \frac{P_i}{P_a}\frac{I_a}{I_i} \qquad (1)$$

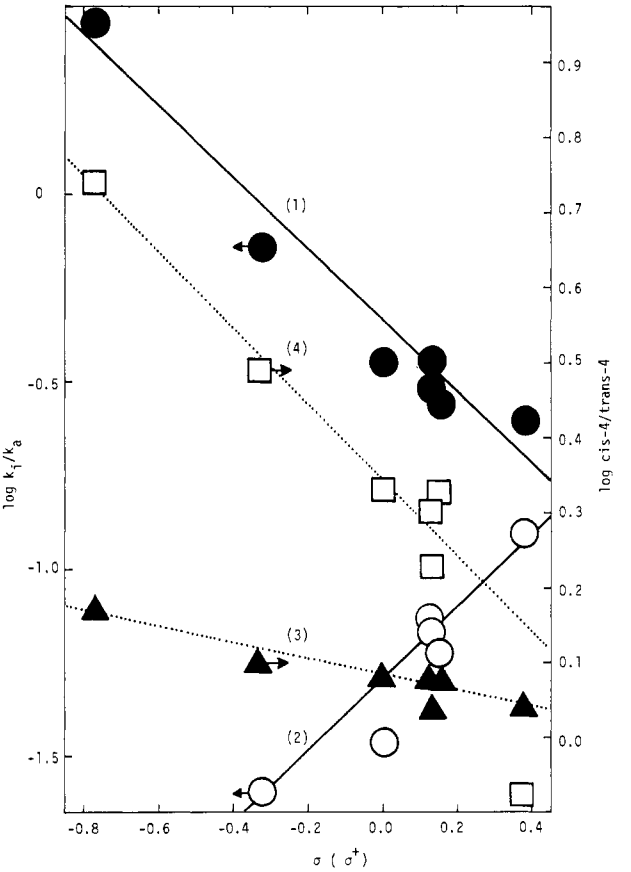


Figure 1. Hammett plots of insertion–addition selectivity [(1) *hν* at 20 °C; (2) Δ at 70 °C] and cyclopropanation stereoselectivity [(3) *hν* at 20 °C; (4) Δ at 70 °C].

the ether (**2**) and cyclopropanes (**4**) and I_a and I_i are the initial moles of olefin and alcohol, respectively. The relative rate constant data correlate well with the Hammett equation using σ (σ+) values

(4) (a) Chang, K.-T.; Shechter, H. *J. Am. Chem. Soc.* **1979**, *101*, 5082. (b) Chambers, G. R.; Jones, M., Jr. *Ibid.* **1980**, *102*, 4516. (c) Recently, intervention of excited carbene was also suggested in the reaction of cyclopropylphenylcarbene: Moss, R. A.; Wetter, W. P. *Tetrahedron Lett.* **1981**, *22*, 997.

(5) Doering, W. von E.; Henderson, W. A. *J. Am. Chem. Soc.* **1958**, *80*, 5274.

(Figure 1), and the ρ value was computed by a least-squares analysis to be −0.96, with a correlation coefficient of −0.96. A similar plot of log {[*cis*-**4**]/[*trans*-**4**]} vs. σ (σ^+) also gives a fairly good correlation and ρ −0.15 (r = −0.95).

Hammett study[6] of the addition of singlet carbenes to substituted styrenes has demonstrated that most simple carbenes are mildly electrophilic in addition to double bonds and that only a perturbed carbene such as cycloheptatrienylidene[6c] undergoes nucleophilic addition. The crucial determination of a ρ value for phenylcarbene addition seems not to have been made, but a similar electrophilic character has been demonstrated[7] in the effect of a carbenic aryl substituent on the isobutene/*trans*-2-butene reactivity ratio. Although there is some ambiguity as to whether singlet carbene is also involved in the present cyclopropanation, due to the lack of a stereochemical "handle" in the olefin employed, a fairly good correlation of cyclopropanation stereoselectivity with σ can be explained[8] only in terms of a transition state for a concerted addition rather than that for stepwise addition. A similar plot of cyclopropanation stereoselectivity, for example, in the photolysis of **1** in *cis*-2-butene gives[8b] a ρ value of −0.35. The OH insertion reaction, on the other hand, is widely accepted[1,9] as a characteristic reaction of a singlet carbene and is generally believed[10] to proceed via initial protonation of the carbene by the alcohol to a carbonium ion and subsequent solvolytic exchange. The observed trends of substituent effects on the insertion–addition selectivities, then, can be reasonably explained in terms of the effect on the transition state for each reaction step of the singlet carbene. Thus, electron-donating substituents moderate the positive charge accumulating on the benzylic carbon as a result of nucleophilic attack on the hydroxylic proton in the OH insertion process, while electron-withdrawing substituents mitigate the accumulation of electrons at the benzylic carbon atom, presumably resulting from partial delocalization of the π electrons of the double bond into the vacant p orbital of the singlet carbene in the addition reaction.

Thermolysis of 1c in the same alcohol–olefin mixture at 70 °C led to a completely different result. Thus, the formation of benzyl ether (**2c**) was greatly suppressed (~3%) and cyclopropane (**4c**) formation became dominant (80%). The insertion–addition selectivity was again sensitive to aryl substituents but the trend of the effect was reversed, as illustrated in Figure 1 (ρ = +1.4, r = 0.93). Correlation of the stereoselectivity with σ also gave a somewhat larger ρ value (−1.1, r = −0.96) but with the same sign. These results could not be explained in terms of electrophilic addition to the olefin and nucleophilic attack on the hydroxylic proton of singlet carbene advanced above. There is a possibility that an increase in the generation temperature of the carbene might affect the carbenic processes by changing the chemical nature of substrate and/or by affecting[11] the activation energy for each process. For example, the acidity of an alcohol is known[12] to change with temperature. This possibility was eliminated by the finding that carbene **6c** generated photolytically at 70 °C from thermally stable precursors, i.e., *cis*- and *trans*-1,2-diphenyloxiranes (**5**),[13] in the binary solvents showed a much larger tendency to insert into the OH bond of alcohol than did **6c** generated at ambient temperature (Table I). The above results clearly indicate that a common intermediate is not involved under both experimental conditions. The intervention of excited diazo compound in the photolytic run was also eliminated since carbene **6** generated from diverse sources (**1** and **5**) at the same temperature yields similar product distributions (Table I). Excited singlet carbenes might be proposed as possible intermediates in the photolytic runs because similar investigations[4] on the effect of generation method on the product distributions suggest that reactions of the excited singlet state may be general, at least for alkylcarbenes generated photolytically. This can be eliminated by the findings that (1) the product ratios are essentially independent of the wavelength employed (e.g., 253 nm for **5** and >300 nm for **1**) and (2) sensitized decomposition of **1** did not alter the product ratios. Changes in wavelength of the incident light should certainly affect the product distributions if a photoexcited carbene intervenes. Moreover, the latter experiment, indicating a rapid triplet–singlet equilibrium,[1] strongly suggested that unexcited singlet carbene generated by intersystem crossing from the triplet ground state is responsible for the reactions. The rather large discrepancy in ρ values for cyclopropanation stereoselectivity between thermal and photochemical experiments implies that a common intermediate is not involved in the cyclopropanation reaction.[14] Apparently, a more probable explanation would be that the free carbene is not involved in the thermal cyclopropanation step, since there have been ample examples[15] indicating that a wide variety of diazoalkanes adds across double bonds to furnish pyrazolines which subsequently eliminate nitrogen to give cyclopropanes at higher temperature. 9-Diazoxanthene, for example, has been shown[16] to react with substituted styrenes with nitrogen evolution at 25 °C to give cyclopropanes, and the rate data give a linear free-energy correlation with ρ = +0.97, indicating that the diazo compound functions nucleophilically. Since no pyrazolines were detected by NMR analysis of the present thermolytic reaction mixtures and since our thermal reactions are completed in <2 h, although phenyldiazomethane requires[17] ca. 1 week to form a pyrazoline with styrene, it might be probable that cyclopropanes

Table I. Effects of Generation Methods on Product Distributions[a]

precursor	T, °C	generation method	relative yield, % 2	*cis*-4	*trans*-4	k_t/k_a
1c	70	Δ	4.2	30.3	65.5	0.035
cis-**5**	70	$h\nu$[b]	52.0	22.6	25.4	0.87
cis-**5**	50	$h\nu$[b]	36.7	24.2	39.1	0.47
trans-**5**	50	$h\nu$[b]	36.3	26.7	37.0	0.46
cis-**5**	25	$h\nu$[b]	32.6	29.4	38.0	0.39
trans-**5**	25	$h\nu$[b]	30.0	33.8	36.2	0.35
1c	25	$h\nu$[c]	30.7	31.3	38.0	0.36

[a] Total product yields are 70–85%. [b] In quartz tube. [c] In Pyrex tube.

(6) For representative additions of carbene to substituted styrenes, see: (a) Seyferth, D.; Mui, J. Y. P.; Damrauer, R. *J. Am. Chem. Soc.* **1968**, *90*, 6182. (b) Sadler, J. *J. Chem. Soc. B* **1969**, 1024. (c) Christensen, L. W.; Waali, E. E.; Jones, W. M. *J. Am. Chem. Soc.* **1972**, *94*, 2118. (d) Stang, P. J.; Mangum, M. G. *Ibid.* **1975**, *97*, 6478.

(7) (a) Closs, G. L.; Moss, R. A. *J. Am. Chem. Soc.* **1964**, *86*, 4042. (b) Moss, R. A. In ref 1a, Vol. I, p 153.

(8) (a) Crumrine, D. S.; Yen, H.-H. B. *J. Am. Chem. Soc.* **1976**, *98*, 297. (b) Moss, R. A. In "Selective Organic Transformations"; Thyagarajan, B. S., Ed.; Wiley: New York, 1970; Vol. I, p 35 ff.

(9) Recent detection and characterization of singlet fluorenylidene provided direct evidence that OH insertion is the characteristic reaction of the singlet: Zupancic, J. J.; Schuster, G. B. *J. Am. Chem. Soc.* **1980**, *102*, 5960.

(10) An alternative but less well-established process includes ylidic attack on the oxygen of the alcohols with protic rearrangement: Bethell, D.; Newall, A. R.; Whittaker, D. *J. Chem. Soc. B* **1971**, 23. Recent studies on the effect of structure on OH insertion also support the carbonium ion mechanism. Thus, for example, electron-donating carbenic aryl substituents favor[10a] OH insertion of arylcarbenes, and 4*H*-imidazoylidenes insert[10b] preferentially into the C–H bond of alcohols. The latter reaction is interpreted as indicating the kinetic barriers in formation of energetic cations: (a) Tomioka, H.; Suzuki, S.; Izawa, Y. *J. Am. Chem. Soc.*, in press. (b) Kang, U.-G.; Shechter, H. *J. Am. Chem. Soc.* **1978**, *100*, 651.

(11) Arylcarbene processes have been shown to be temperature dependent for the reactions with olefin[11] and alcohol:[11b] (a) Moss, R. A.; Joyce, M. A. *J. Am. Chem. Soc.* **1978**, *100*, 4475 and references cited therein. (b) Tomioka, H.; Izawa, Y. *Ibid.* **1977**, *99*, 6128.

(12) See, for example: (a) Hirayama, S. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2653. (b) Ellis, A. J. *J. Chem. Soc.* **1963**, 2299.

(13) For a review of carbene formation from oxiranes, see: Bertoniere, N. R.; Griffin, G. W. In ref 1a, Vol. I, p 305.

(14) Stereoselectivity has been shown[7b] to be sensitive to the intermediates involved. For example, the carbenoid exhibits a greater syn stereoselectivity than the free (photolytic) carbene.

(15) Wulfman, D. S.; Linstrumelle, G.; Cooper, C. F. in "The Chemistry of Diazonium and Diazo Groups"; Patai, S., Ed.; Wiley: New York, 1978; Vol. II, p 821.

(16) Jones, G. W.; Chang, K.-T.; Munjal, R.; Shechter, H. *J. Am. Chem. Soc.* **1978**, *100*, 2922.

(17) Overberger, C. G.; Weinshenker, N.; Anselme, J.-P. *J. Am. Chem. Soc.* **1965**, *87*, 4119 and references cited therein.

Table II. NMR Spectra (δ) of 4a-g

compd	Ar	EtO*CH*	ArCH	CH_2	OCH_2	OCH_2-CH_3	other
4a (*p*-MeO)	7.8-6.6	3.30	1.90	0.9	3.55	1.20	3.70
					3.30	0.96	
4b (*p*-Me)	7.3-6.8	3.20	1.80	0.9	3.49	1.12	2.28
					3.24	0.98	
4c (*p*-H)	7.2-6.9	3.45	1.90	0.9	3.60	1.20	
					3.45	1.00	
4d (*p*-Cl)	7.4-6.8	3.30	1.90	1.1	3.54	1.20	
					3.25	1.00	
4e (*m*-MeO)	7.1-6.4	3.40	1.85	1.0	3.50	1.19	3.73
					3.25	0.93	
4f (*p*-Br)	7.5-6.8	3.28	1.85	0.9	3.50	1.18	
					3.35	0.98	
4g (*m*-Cl)	7.1-6.4	3.39	1.85	1.0	3.55	1.15	
					3.20	0.93	

may be formed directly via nucleophilic attack of **1** accompanied by loss of nitrogen.

Experimental Section

IR spectra were recorded on a Jasco IR-G recording spectrometer. ^1H NMR spectra were determined on a JEOL JNM-MH-100 spectrometer as $CDCl_3$ solutions with an internal $(CH_3)_4Si$ standard. GC-MS spectra were obtained on a Shimadzu GC-MS 1000 spectrometer using a column consisting of silicone OV-17 on Shimalite (4.0 mm × 2.0 m). GC work was done on a Yanagimoto G-180 gas chromatograph using a 4.0 mm × 2.0 m column packed with OV-17 (5%) on 60-80 mesh Diasolid L.

Materials. The aryldiazomethanes **1a-g** were prepared according to literature procedures[18] immediately before use. Authentic samples for identification of reaction products were synthesized as follows. Most of the ethers **2** were conveniently prepared by a Williamson synthesis. Commercially unavailable C-H insertion products were prepared by Grignard reaction of the corresponding ketone with CH_3MgI. Satisfactory spectroscopic data have been obtained for all authentic samples. The cyclopropanes **4** were isolated from the irradiation mixture by GC and identified by NMR and MS. The configuration of the cyclopropanes has been assigned on the basis of the NMR arguments[7a] that the trans-ethoxy protons should be deshielded by the anisotropy of the phenyl ring while the cis-ethoxy protons should show an increased shielding. Equilibration experiments of the two epimeric adducts by treatment with potassium *tert*-butoxide in $(CH_3)_2SO$ also support the assignment. NMR data for *cis*- and *trans*-**4** are given in Table II.

Photochemical Reactions and Analyses. All irradiations were carried out with a Halos 300-W high-pressure mercury lamp with a water-cooled jacket. In a typical procedure, 0.005 mmol of the diazo compounds was added to 2.0 mL of a binary mixture of 2-propanol and ethyl vinyl ether in Pyrex tubes. The sample was then degassed, sealed, and suspended in a transparent Dewar thermostated at the appropriate temperature. Irradiation was generally continued until all of the diazo compound was destroyed. Sensitized experiments were performed under conditions similar to those described above. Usually a 50 M excess of benzophenone to the diazo compound was added to ensure that >95% of the incident light was absorbed by the sensitizer. That addition of benzophenone greatly accelerates the rate of decomposition was noted. Irradiation of oxirane **5** was carried out in a quartz tube. Thermolysis was done in a sealed Pyrex tube. Control experiments exclude possible conversion of the products during the decomposition period and also demonstrate that no reactions occur in the absence of light in the photolysis of **1** and **5** over the temperature range studied.

Product identifications were established either by GC or by GC-MS comparisons using authentic samples. Product distributions were conveniently determined by standard techniques.

Registry No. **1a**, 23304-25-8; **1b**, 23304-24-7; **1c**, 766-91-6; **1d**, 19277-54-4; **1e**, 65864-99-5; **1f**, 73900-14-8; **1g**, 51157-54-1; *cis*-**4a**, 80287-83-8; *trans*-**4a**, 80287-84-9; *cis*-**4b**, 40237-67-0; *trans*-**4b**, 40489-59-6; *cis*-**4c**, 80287-85-0; *trans*-**4c**, 80287-86-1; *cis*-**4d**, 80287-87-2; *trans*-**4d**, 80287-88-3; *cis*-**4e**, 80287-89-4; *trans*-**4e**, 80287-90-7; *cis*-**4f**, 80287-91-8; *trans*-**4f**, 80287-92-9; *cis*-**4g**, 80287-93-0; *trans*-**4g**, 80287-94-1; *cis*-**5**, 1689-71-0; *trans*-**5**, 1439-07-2.

(18) Creary, X. *J. Am. Chem. Soc.* **1980**, *102*, 1611.

Synthesis and Characterization of an Oligonucleotide Containing a Carcinogen-Modified Base: O^6-Methylguanine[1]

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Abstract: The synthesis and characterization of the oligomer 5′-dTp(O^6-Me)GpCpA-3′ by the modified triester procedure is described, representing the preparation of a DNA fragment containing a base specifically covalently modified by a carcinogen. With use of the tools of genetic engineering, this tetramer will be substituted for a 5′-TpGpCpA-3′ portion of the DNA of bacterial virus *φX174* in order to study the effect on replication of a well-characterized chemical modification of DNA at an exactly known point. The presence of O^6-methylguanine in the oligomer is shown to inhibit the enzyme activities of snake venom phosphodiesterase and endonuclease P_1.

The formation of chemical carcinogen-DNA adducts may induce changes in DNA base sequence and, ultimately, neoplastic transformation. However, despite the growing body of literature which describes the formation and structure of a number of adducts (such as those derived from aflatoxin B_1,[3] sterigmatocystin,[4] benzo[*a*]pyrene,[5] and acetylaminofluorene[6]), no correlation has been established between the structure of an adduct, its location in a gene, and the mutagenic risk it poses to the cell. Previous studies on the mechanism of mutagenesis have been constrained by the inability to produce a lesion at a particular site, to determine

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