uniformity of the capillary bore were determined by measurement of the length of mercury columns and weighing the mercury; the diameter was found to be 1.005 mm. The flask is initially filled through the open joint with the methanolic dye solution (0.006 M); the 0.5-mL syringe, which had been ground to fit the joint, was filled with lithium methoxide in methanol (1.4 M; lithium was chosen because of the relatively high solubility of its perchlorate in methanol). The insertion must be done with care so that the needle is in the protuberance of the flask and such that no air bubbles are trapped. The methanolic dye solution rises somewhat into the capillary while this is done. Some epoxy adhesive is applied to the joint, since otherwise evaporation through the annular space between flask and syringe is a significant problem. The assembly is then thermostated, and the 0.5-mL syringe is emptied very slowly (during about 1 min), so that no significant mixing occurs. Then the level is adjusted to a desired level by means of another hypodermic syringe and read by means of suitable magnification. The magnetic stirrer is activated and left on for ~0.5 min, causing complete decolorization of the solution. The level undergoes a rapid rise during this time and then slowly falls again as the heat liberated by the reaction is liberated. It eventually (after 10–15 min) declines to a very slow constant rate caused by evaporation. Extrapolation of this very slow decline back to the time of mixing gives the corrected final reading. In order to do the experiment in a reasonably short time, the lithium methoxide was somewhat in excess. The dilution of the base produced a volume decrease which was evaluated independently. A correction for this effect was made; the calculation, too obvious to require recording here, shows that the reaction volume could be determined in this way with a reproducibility less than 1 cm^3/mol.

The kinetics were followed at 25.00 ± 0.05 °C by means of a Cary 14 in an Aminco high-pressure optical cell with quartz windows, fitted with a cylindrical quartz sample cell, with mercury providing the flexible separation between hydraulic fluid (water–glycerin, 1:1 v/v) and reaction solution.[20] The pH of the solutions was measured by means of a Beckman research pH meter and a Duramark "pencil" combination electrode (Markson Scientific); this equipment was calibrated with standard buffers to ±0.001 pH unit.

The Dabco–perchlorate buffer was prepared according to a standard procedure.[21] The buffer base concentration was 2.0×10^{-3} M in all runs, and the ionic strength was maintained at 8.4×10^{-3} M by the addition of $KClO_4$ to the solutions. A 4×10^{-4} M master solution of Malachite Green tetrafluoroborate was prepared in anhydrous methanol containing a small amount of hydrochloric acid. A 1-mL portion of this solution was added to 9 mL of buffer and the kinetics were followed at 610 nm. All the reactions were followed for a minimum of 6 half-lives; the end absorbance was read after 12 half-lives. The pH of the reaction mixture was measured at regular intervals and found to be constant within ±0.01 pH unit. Pseudo-first-order rate constants were calculated from the slope of the plot ln $(A_t - A_\infty)$ vs. time, where A_t is the absorbance at time t and A_∞ is the end absorbance. All the data were subjected to least-squares fits.

Acknowledgment. The National Science Foundation has generously supported this work. We have carried on an occasional, decade-long correspondence about this problem with Professor C. D. Ritchie, whom we thank for his interest and comments. Ms. L. Ferry is thanked for carrying out some of the initial exploratory work.

Registry No. Malachite Green tetrafluoroborate salt, 60885-33-8; Dabco, 280-57-9; DabcoHCl, 2099-72-1; *p*-quinone, 106-51-4; *p*-dimethoxybenzene, 150-78-7.

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[20] W. J. le Noble and A. R. Das, *J. Phys. Chem.*, **74**, 3429 (1970).

[21] R. g. Bates, "Determination of pH: Theory and Practice", Wiley, New York, 1964.

Temperature and Substituent Effects on Regioselectivity in the Insertion of Arylcarbene into Alcohols[1]

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Abstract: Photolysis of aryldiazomethanes in methanol, ethanol, and 2-propanol gave OH insertion products along with small amounts of CH insertion products at ambient temperature. However, the CH insertion products increased significantly at the expense of the ether as the temperature was lowered. The attempted sensitized decomposition of the diazomethane did not lead to an increase in the CH insertion products presumably because of a rapid singlet–triplet equilibrium. The key intermediate leading to the CH insertion is suggested to be ground-state triplet arylcarbene, based on the accumulated spectroscopic as well as chemical evidence for the intervention of the triplet arylcarbene in the low-temperature photolysis of aryldiazomethanes. Substituents on the phenyl ring also have an appreciable effect on the insertion selectivity. At room temperature, the OH/CH insertion selectivity increased with the electron-donating ability of the substituents. This is interpreted in terms of the substituent effect on the transition state of OH insertion, where there is a deficiency of electrons at the benzylic carbon atom, rather than on the stability of singlet carbene. At low temperature, both electron-donating and -withdrawing substituents facilitate OH insertion, indicating that the change in substituents induces a concomitant change in the insertion mechanism, presumably due to decreasing nucleophilicity of carbene with increasing electron-withdrawing ability as well as decreasing proton–donor activity of alcohol with decreasing temperature. This may also reflect the effect of the substituent on the singlet–triplet energy gap.

Carbene chemistry is of interest to both mechanistic and synthetic organic chemists especially on the subject of spin states and intrinsic reactivity. Although the current era of carbene chemistry began with the recognition of the two characteristic carbene reactions, insertion into C–H bonds and addition to C–C double bonds, the most widely used diagnostic for spin state has been the latter reaction.[2] This is because of a stereochemical label to distinguish between the concerted (singlet) and stepwise (triplet) nature of the addition reaction. A mechanistic ambiguity on the exact multiplicity responsible for CH insertion was recognized since abstraction of a hydrogen atom followed by coupling of the radical pair could give rise to the same products as concerted

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[1] (a) Carbene in Rigid Matrix. Part XII. (b) For a preliminary description of the present work, see: Tomioka, H.; Izawa, Y. *J. Am. Chem. Soc.* **1977**, *99*, 6128.

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

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insertion. Many efforts have been made, however, to clarify these problems, and many important results are now available[3] on the nature of the C–H insertion reaction from studies of stereochemistry, insertion selectivity, and direct spectroscopic data (e.g., CIDNP and ESR). Particular attention has been given to the reaction of carbenes with heteroatomic compounds in the hope that most singlet carbenes are electrophilic and will selectively attack the unshared electrons on the heteroatom. This forms ylides which undergo subsequent reactions.[4] For example, it has been shown[5] that in the reaction of carbonyl carbene with allyl compounds containing a heteroatom, e.g., allyl halide, attack of singlet carbene on a lone pair proceeds several times faster than attack on the π bond of an olefin and that the triplet state cannot interact with unshared electrons. The reaction of carbene with alcohol has also attracted much attention in this connection. Most of the nascent (singlet) carbene generated in alcoholic solution predominantly inserts into the OH bond, rather than into the C–H bonds of the alcohol.[4] Hence the detection of ethers in an alcoholic reaction system in which carbene may be involved is strong evidence[6] for the intervention of carbene intermediate. A recent pulsed-laser spectrophotometric investigation[7] of the chemistry of fluorenylidene in solution phase provided direct evidence that the OH insertion is the characteristic reaction of the singlet. A few carbenes, e.g., vinylidenes[8] and 4*H*-imidazoylidenes,[9] have been reported to insert effectively into C–H bonds of alcohols even when they are generated in alcoholic solution at ambient temperature. The anomalous behavior of these unique carbenes has been explained in terms of special orbital interactions. The interaction of singlet vinylidene with the OH bond of an alcohol orients the carbenic center in close proximity to the C–H bonds. Kinetic hurdles have been invoked in the formation of an energetic intermediate (i.e., carbonium ion), leading to OH insertion of singlet 4*H*-imidazoylidene. The reactions of triplet carbene with alcohol are, on the other hand, generally supposed[10] to proceed through initial abstraction of hydrogen from the CH bonds of the alcohol. This is in view of the large dissociation energy of the OH bond and leads to several "radical products", e.g., double-hydrogen abstraction product and/or C–H "insertion" products. While a greater number of mechanisms are possible for the OH insertion reaction in principle, chiefly three mechanisms have been discussed: (a) protonation of the carbene to give carbonium ions,[11] (b) electrophilic attack of the carbene at oxygen, followed by proton transfer,[12] and (c) one-step insertion into the O–H bond.

In order to throw additional light not only on the mechanism of OH insertion of arylcarbene but also on the relation between reaction pattern and multiplicity in the arylcarbene reaction with alcohols, the effects of temperature and aryl substituents on the reaction were investigated. The results revealed that (i) insertion selectivities (OH/CH as well as tertiary/secondary/primary CH) are highly sensitive to the temperature of the generation of carbene, (ii) ground-state triplet arylcarbenes are responsible for the CH insertion especially at lower temperature, and (iii) the carbonium ion mechanism is prevailing for OH insertion at ambient temperature but both carbonium ion and ylide mechanisms seem to be operating at lower temperature.

Table I. Temperature Dependence of Product Distributions in the Photolysis[a] of **1** in Alcohols

ROH[c]	*T*, °C	relative product yields, %[b]				
		2	**3**	**4**	**5**	**6**
MeOH	0	92.6	3.4	2.8	1.2	
	−78	90.3	2.3	3.5	3.9	
	−110	74.0	4.3	1.0	20.7	
	−155	62.9	4.8	1.0	31.3	
	−196	52.9	6.0	0.8	40.3	
EtOH	0	87.1	5.0	3.3	4.6	*d*
	−78	82.7	4.6	2.0	10.7	*d*
	−110	74.1	5.0	1.9	17.8	1.2
	−155	42.3	6.3	1.1	47.4	2.9
	−196	20.8	9.8	0.4	64.2	4.8
i-PrOH	0	72.4	3.8	6.7	16.6	0.5
	−78	51.5	5.8	13.7	28.1	0.9
	−110	35.7	5.2	2.0	46.3	10.8
	−155	19.8	5.0	1.5	59.8	13.9
	−196	14.7	5.6	1.3	63.8	14.6

[a] Irradiations were performed on a 2.5 mM solution of **1**. Irradiations performed in the solid phase were conducted over 4-h intervals without thawing the matrix in the dark (see also Experimental Section). [b] Data are expressed as percentages (based on the average of duplicate runs) of products **2–6**, normalized to 100%. Total product yields are ~70–80% over the temperature ranges studied. Other products were benzaldehyde, aldazine, and stilbenes. [c] The melting points of pure methanol, ethanol, and 2-propanol are −97.8, −114.1, and −88.5 °C, respectively. [d] Trace.

Table II. Temperature Dependence of Product Distributions in the Photolysis[a] of **7** in Alcohols

ROH[c]	*T*, °C	relative product yields, %[b]			
		8	**9**	**10**	**11**
MeOH	0	>99	<1	0	
	−78	>99	<1	0	
	−110	97.8	2.2	*d*	
	−155	94.8	2.5	2.7	
	−196	62.0	3.0	35.0	
EtOH	0	97.6	2.4	*d*	*d*
	−78	97.4	2.5	0.1	*d*
	−110	97.2	2.6	0.2	*d*
	−155	90.1	3.6	6.0	0.3
	−196	46.9	2.8	36.7	13.6
i-PrOH	0	92.2	7.7	0.1	*d*
	−78	89.9	9.8	0.3	*d*
	−110	86.7	4.9	7.7	0.7
	−155	57.0	4.8	37.5	0.7
	−196	30.1	5.3	49.9	14.7
	−196[e]	36.2	4.6	49.7	8.5

[a] See footnote *a* in Table I. [b] Data are expressed as percentages (based on the average of duplicate runs) of products **8–11**, normalized to 100%. Total product yields are 70–85%. Other products were benzophenone, tetraphenylethane, and ketazine from **7**. [c] See footnote *c* on Table I. [d] Trace. [e] Irradiation was interrupted at 10-min intervals for thawing the matrix in the dark.

Results and Discussion

Effects of Temperature. Solutions of monophenyldiazomethane (MPD, **1**) in degassed alcohols were irradiated in Pyrex tubes (λ >300 nm) at different temperatures as detailed in the Experimental Section. GC analysis of the product mixture revealed the presence of OH insertion products (**2**) and two CH insertion products (**5** and **6**), along with small amounts of toluene, bibenzyl, and aldazine (eq 1). The identities of these products were established by GC–MS chromatographic comparison with authentic samples. The product distributions were determined by GC analysis using mechanical integration and appear in Table I as a function of temperature. As is evident from the table, the product distributions were highly dependent on the temperature at which monophenylcarbene (MPC) was generated. Photolysis of **1** in 2-propanol at room temperature, for example, gave the ether **2c** as almost exclusive product (81%). When the photolysis

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[3] Gasper, P. P.; Hammond, G. S. In ref 2b, Vol. II, p 310 ff.

[4] See, for example: Kirmse, W. In ref 2a, p 407 ff.

[5] Ando, W.; Kondo, S.; Nakayama, K.; Ichibori, K.; Kohoda, H.; Yamato, H.; Imai, I.; Nakaido, S.; Migita, T. *J. Am. Chem. Soc.* **1972**, *94*, 3870, and references cited therein.

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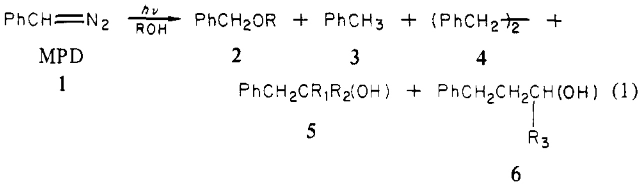
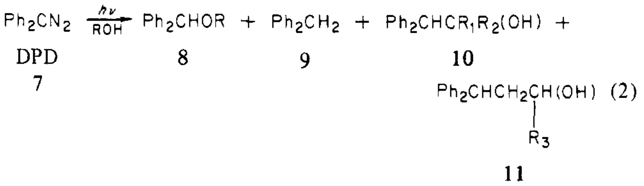


$$\underset{\substack{\text{MPD}\\ \mathbf{1}}}{PhCH{=}N_2} \xrightarrow[ROH]{h\nu} \underset{\mathbf{2}}{PhCH_2OR} + \underset{\mathbf{3}}{PhCH_3} + \underset{\mathbf{4}}{(PhCH_2)_2} + \underset{\mathbf{5}}{PhCH_2CR_1R_2(OH)} + \underset{\mathbf{6}}{PhCH_2CH_2\underset{R_3}{CH}(OH)} \quad (1)$$



$$\underset{\substack{\text{DPD}\\ \mathbf{7}}}{Ph_2CN_2} \xrightarrow[ROH]{h\nu} \underset{\mathbf{8}}{Ph_2CHOR} + \underset{\mathbf{9}}{Ph_2CH_2} + \underset{\mathbf{10}}{Ph_2CHCR_1R_2(OH)} + \underset{\mathbf{11}}{Ph_2CHCH_2\underset{R_3}{CH}(OH)} \quad (2)$$

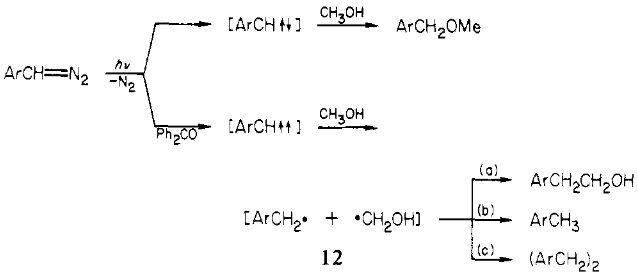
a, R = Me: $R_1 = R_2 = H$; b, R = Et, R_1 = Me, $R_2 = R_3 = H$; c, R = *i*-Pr; $R_1 = R_2 = R_3$ = Me

was carried out at −196 °C, however, the C–H insertion products (**5c**, 68.4%; **6c**, 15.8%) dramatically increased at the expense of the OH insertion product. A parallel series of irradiations in methanol and ethanol also showed that a similar temperature dependence of the regioselectivity of carbene insertion into alcohols is quite general in each system studied. Diphenyldiazomethane (**7**) showed similar behavior (eq 2, Table II).

It is generally accepted[2,13] that alcohols react with carbene in the singlet state to give OH insertion product. A recent pulsed-laser spectroscopic analysis[7a] of transient products in the chemistry of fluorenylidene (Fl) in alcohol–acetonitrile solution shows that, while a short-lived intermediate attributable to ^{1}Fl reacts with methanol quite rapidly, ^{3}Fl reacts very slowly with methanol and, as the methanol content increases, the amount of ^{3}Fl formed decreases, becoming zero at high methanol concentration. Photolysis of **1** in neat methanol at ambient temperature gave almost exclusively benzyl ether (**2**). This suggests that singlet carbene (^{1}MPC) is also responsible for the OH insertion in the present reaction. Support for the intermediacy of free carbene is provided by the observation[14] that irradiation of either **1** or *cis*- and *trans*-2,3-diphenyloxiranes (DPO)[15] at room temperature yields experimentally indistinguishable product distributions in each alcohols.

Now the question is which multiplicity is responsible for the emerging dominance of the C–H insertion products in the low-temperature experiments? Apparently, the specific orbital interaction of carbene with the OH bond of the alcohol and the energetic problems suggested[8,9] to explain the dominant formation of C–H insertion from singlet vinylidene and 4*H*-imidazoylidene seem to be unimportant in arylcarbenes. The potential intervention of reactions of excited diazo compounds masquerading as carbene is reduced by the findings[14] that low-temperature photolysis of a nitrogen-free precursor, i.e., DPO, in alcohol also resulted in a marked increase in C–H insertion products. There are several examples,[2,10] on the other hand, that triplet arylcarbene abstracts hydrogen from the C–H bonds of alcohols to give radical pairs (**12**), which subsequently undergo three competing reactions: (a) recombination to the C–H "insertion" product, (b) abstraction of a second hydrogen to give a double-hydrogen abstraction product, and (c) dimerization to a radical dimeric product, as depicted in the Scheme I. It was possible[7c,16] to generate the triplet arylcarbene in solution by selectively exciting benzophenone in the presence of **1** by using a Corning CS-052 filter (>350 nm) so as to assure absorption of 99% of the incident light by the photosensitizer. The product ratios were not altered, however, by the addition of a large excess of Ph$_2$CO (see Table III). Evidence that Ph$_2$CO does indeed serve as a photosensitizer for decomposition of **1** to MPC is clear from the acceleration in the decomposition rates observed as the concentration of this ketone is increased, not only in fluid but in rigid media as well. This is not unreasonable in light of the facile singlet–triplet equilibration mechanism[7c,10,13] available for most arylcarbenes. It has been demonstrated,[17] however, that most arylidazo compounds, when photolyzed in organic matrices at −196 °C, give triplet carbenes which can be detected spectroscopically and show the chemical behavior expected from triplet carbenes upon thawing, e.g., hydrogen–abstraction and reaction with oxygen. Further, Moss et al.[18] have shown that stereospecific cyclopropanation observed in the photolysis of aryldiazo compounds in olefin solution became less important when the photolysis is carried out in a frozen olefinic matrix at −196 °C. Instead, large amounts of olefin were formed, which were shown to arise by an abstraction–recombination (a–r) reaction of the triplet arylcarbene. More importantly, Platz et al.[19] have studied the decay rates of ^{3}DPC and ^{3}Fl in various organic matrices, including alcohols, by ESR. They have shown that the decay rates are sensitive to the chemical nature as well as the viscosity of the matrix, indicating that the reactions of ^{3}DPC and ^{3}Fl with the host molecules are occurring. They have actually demonstrated that the predominant decay pathway of the triplet carbene is hydrogen atom tunneling as is evident from very low Arrhenius parameters and anomalous isotope effects. From these precedent facts we suggest that the key intermediate leading to the CH insertion products in the solid-phase experiments is also triplet carbene and that the CH "insertion" products are derived via the a–r mechanism rather than direct insertion. The observation that the other possible products derived from free benzyl radical, such as toluene or bibenzyl, were not appreciably increased with increasing C–H "insertion" products reflects the mobility of members of radical pairs in the solid state. Thus, as the temperature is lowered, recombination of the radical pairs (**12**) leading to CH "insertion" becomes more efficient compared to the diffusion to free radical due to increasing viscosity[20] of the environment with decreasing temperature.

Scheme I



Supporting evidence emerges from the effect of carbenic substituents on the temperature dependency of the reaction with alcohols. Thus, photolysis of other more complicated aryldiazo compounds (**13a**,[21a] **13b**,[21b] **13c**,[21a] **13d**,[21c] and **13e**,[21c]) in alcohol matrix at −196 °C also resulted in a marked increase in the CH insertion products at the expense of the other major product resulting from room-temperature photolysis. It should be pointed

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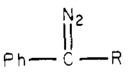
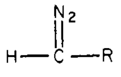


$\mathrm{Ph{-}C({=}N_2){-}R}$

13

a, R = CO_2Me; b, R = $P(O)(OMe)_2$
c, R = COPh; d, R = CH_3
e, R = CH_2Ph



$\mathrm{H{-}C({=}N_2){-}R}$

14

a, R = CO_2Me; b, R = COPh

out that photolysis of **13c–e** at −196 °C gave ground-state triplet ESR signals.[17] Interestingly, the displacement of a phenyl group on carbenic carbon by hydrogen markedly changed[21a,22] the temperature dependency of the product distributions. Carbene from **14** showed only a slight increase in CH insertion. It is important to note that the triplet state of $:CHCO_2Me$ is shown[23] to be very reactive and that conversion to a more reactive state is rapid even at 40 K. This implies that the −196 °C matrix is not cool enough to populate triplet $:CHCO_2Me$ by quenching the singlet reaction.

The reason for the marked reduction of the OH insertion at lower temperature is then an important question. In their temperature studies[18c] of the reactions of DPC with isobutylene, Moss et al. have found that the logarithm of the C–H insertion/cyclopropanation product ratio varies linearly with T^{-1} through liquid to solid runs. They have interpreted these results in terms of simple temperature effect on kinetics of the competitive singlet and triplet carbene processes. Similar plots of ln OH insertion/H abstraction product ratio with T^{-1} shown in Figure 1 indicated that the ratio decreases rather steadily as the temperature decreases. This is in marked contrast to that observed[24] for similar plots of C–H insertion selectivities of MPC into alkane, which shows inversion in the graph as the reaction phase changes from liquid to solid. The phenomenon has been interpreted as indicating that a matrix imposes severe steric demands on the reactions of carbenes within it. Since there is no obvious discontinuity (or inversion) in the present graph through liquid to solid runs, matrix effects may not be rigorously affecting the OH/CH insertion selectivity in the matrix. This can be interpreted as reflecting a simple temperature effect on an equilibrated singlet and triplet arylcarbene system[25] if one assumes that the mechanisms of each insertion reactions do not change throughout the temperature ranges studied. This seems unlikely since such large changes in the temperature and reaction phases should cause a change in the reaction pathway (vide infra). For example, Campion and Williams[26a] observed that the Arrhenius parameters for reaction of methyl radicals with methanol changed with temperature and phase. The activation energy and log A value were 0.9 kcal/mol and 0.041 s^{-1}, respectively, in a viscous alcoholic glass, whereas the solution values were 8.2 kcal/mol and 14 s^{-1}, respectively. This has been interpreted as indicating that as the reaction temperature is lowered the classical reaction rate becomes much slower than decay by hydrogen atom tunneling. The kinetic studies of Platz[19a,b] and Gaspar[19c] have shown that hydrogen-atom abstraction of triplet carbene from the matrix is also quantum-mechanical tunneling in nature. It is reasonable to suggest that the hydrogen-atom abstraction–recombination products increase at lower temperature since tunneling should become relatively important as the reaction temperature is decreased.[26b]

Finally, it is important to know the exact temperature at which reactions occur, especially in the matrix. The significant differences in the results between the −155 and −196 °C matrix suggest that most of the product formation occurs in the matrices at the photolysis temperature. We observed, however, that insertion ratios were relatively sensitive to the period of irradiation–thaw cycles (see Table II). When the irradiation performed in the −196 °C 2-propanol matrix was interrupted at 10-min intervals for thawing in the dark until all of DPD was consumed, the product ratios of OH/CH (0.57) as well as α-CH/β-CH (5.85) insertion increased appreciably compared to those obtained (0.43 and 3.40, respectively) in the run where low-temperature irradiation was conducted over 4-h intervals without thawing the matrix. This implies that some of triplet arylcarbene reacts very slowly with the matrix at −196 °C and reacts at higher temperatures when the matrix is thawed in the dark. Kinetic studies[19] also show that some aryl carbenes react very sluggishly at −196 °C.

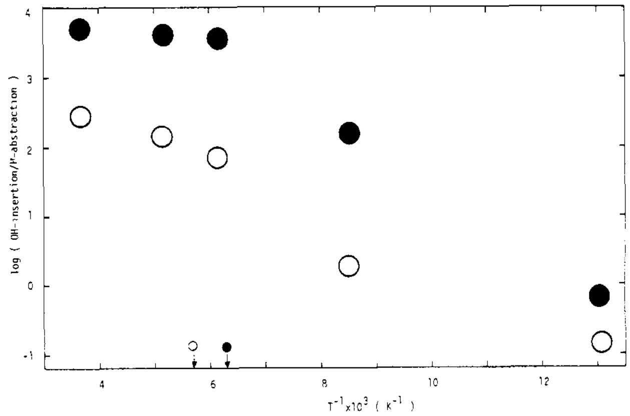
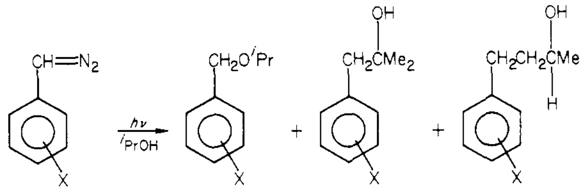


Figure 1. Product ratios as a function of temperature in the photolysis of **7** in ethanol (●) and 2-propanol (○). The points marked ○ and ● show melting points of ethanol and 2-propanol, respectively.

Effect of Aryl Substituents. In order to explore further the nature of each insertion process, it might be quite fruitful to study the effects of aryl substituents on the arylcarbene reactions with alcohol. To date, a limited number of arylcarbene selectivities have been investigated in terms of substituent effects. These studies have been successfully applied to studies of reaction mechanisms involving other important carbon intermediates, i.e., carbonium ion, free radical, and carbanion. Quantitative correlations between structure and reactivity of carbenes have been the subjects of increased interest, and many pertinent facts as to the nature of the carbene reaction are now available. Again, most of these studies have treated the addition[27,28] of carbene to olefins, and only a limited number of studies have been devoted to the nature of CH insertion.[12,29] Thus, a series of monoaryldiazomethanes (**15**) were irradiated in i-PrOH at 0 and −196 °C. Table III gives the results of these studies in terms of the OH insertion to CH "insertion" ratio.



15 16 17 18

Consider first the ambient-temperature irradiation experiments. In all cases, the OH insertion product (**16**) is produced as the main

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(25) According to the Moss's treatment,[18] we estimate $\Delta E^{a}_{app(arent)}$ for the DPC–i-PrOH reaction to be 1700 cal/mol from the observed insertion/abstraction ratios at 0 and −196 °C. Neglecting triplet OH insertion process and taking an upper limit of 3 kcal/mol for the differential singlet–triplet energy (ΔE_{ST}),[13] a value of <1.3 kcal/mol was obtained for ($E^{a,T}_{abst} - E^{a,S}_{insert}$). This indicates that the activation energy for triplet abstraction is greater by 1.3 kcal/mol than that for singlet insertion, but this difference is smaller than the energy difference between the singlet and triplet states of DPC. Thus, as the reaction temperature is lowered, triplet abstraction gains relative to singlet insertion.

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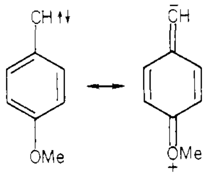
Table III. Effect of Substituent on Product Distribution in the Photolysis[a] of Monoaryldiazomethanes (**15**) in 2-Propanol at 0 and −196 °C

	product distributions[b] at							
	20 °C rel yield, %			**16**	−196 °C rel yield, %			**16**
X in **15**	**16**	**17**	**18**	**17** + **18**	**16**	**17**	**18**	**17** + **18**
a, *p*-MeO	97.6	2.4	*c*	40.7	82.8	15.2	2.0	4.82
(*p*-MeO[d]	>99	<1	*c*	99	82.7	15.5	1.8	4.78)
b, *p*-Me	95.5	4.5	*c*	21.2	39.1	47.1	13.8	0.64
c, H	90.7	9.3	*c*	9.75	15.8	68.5	15.7	0.19
(H[d]	93.9	6.1	*c*	15.3	15.6	68.8	15.6	0.21)
d, *p*-Cl	87.2	12.8	*c*	6.81	28.3	49.8	21.9	0.39
e, *m*-MeO	90.5	9.5	*c*	9.53	32.6	45.1	22.3	0.48
f, *p*-Br	87.1	12.9	*c*	6.75	30.6	46.0	23.4	0.44
(*p*-Br[d]	93.7	6.3	*c*	14.9	30.9	47.0	22.1	0.45)
g, *p*-CO_2Me	86.4	12.5	1.1	6.35	47.7	32.0	20.3	0.91
h, *p*-CN	79.5	17.8	2.7	3.88	50.6	34.0	15.4	1.02

[a] See footnote *a* in Table I. [b] Data are expressed as percentages (based on the average of duplicate runs) of insertion products (**16**–**18**), normalized to 100%. Total product yields (~70%) are essentially invariant regardless of temperature as well as substituents. Although substituted toluenes and bibenzyls were detected (~5%) in each run, the quantification was not made for all aryldiazomethanes employed because of difficulties encountered in the separation, but inclusion of the yield of these compounds in the numerator did not change the trend of substituent effects. [c] Trace. [d] A 50-molar excess of Ph_2CO added as a triplet sensitized.

product, but the product ratio is substituent dependent. Electron-donating substituents such as *p*-Me and *p*-MeO lead to more ether, while C–H insertion slightly increases in the case of electronegative substituents. A plot of log [**16**/(**17** + **18**)] vs. σ (σ^+ for electron donor group) gives a fairly linear correlation (r = 0.98) (Figure 2). A similar approach[30] in the competitive addition of ArCH: to 1,1-dimethylallenes also revealed the linear relationship of singlet–triplet reaction product ratio with σ (σ^+), singlet-derived product being favored by electron-donating substituents. This behavior has been interpreted[30] as being indicative of the substituent effect on the singlet carbene stability. It is suggested that increased stability of the singlet carbene is derived from delocalization as in **19** with increasing electron release. In a similar manner, singlet carbenes with electron-withdrawing substituents are not stabilized by this electronic interaction in the planar conformation. A similar interpretation can be applied to explain the present data since the direction of substituents on the singlet/triplet product ratio is also the same. However, the recent elegant studies on thermal decomposition rates[31] of substituted DPD as well as the stereochemistry[32] of rearrangement of substituted 1-phenyl-1-propylidenes by Shechter et al. have demonstrated that electron-donating para substituents favor a planar conformation for a singlet carbene in order to stabilize its electron-deficient, carbene p orbital, but that electron-withdrawing para substituents are presumed to enhance twisting of the phenyl group to a perpendicular conformation in which the electron-rich, carbene σ orbital is also favorably delocalized. Calculations of net atomic charges of para-substituted singlet phenylcarbenes also supported the possible interaction of their nonbonded orbitals with both types of substituents. An alternative and more likely explanation would be, then, that the observed substituent effects reflect the effect on the transition state of each insertion step. The fact that Ph_2CO-sensitized composition of para-unsubstituted, *p*-methoxy-, and *p*-bromophenyl-diazomethane in *i*-PrOH yields experimentally indistinguishable values of OH/CH insertion ratios at 0 and −196 °C indicates that singlet–triplet equilibration is faster than reactions of the carbene with alcohol. Assuming that the hydrogen abstraction reaction of free radicals is relatively insensitive to polar effects,[33] the increase in OH insertion with increasing electron release by substituents is expected from the carbonium ion mechanism in which electron-releasing substituents moderate the positive charge accumulating on the benzylic carbon as a result of nucleophilic attack with the electron-rich σ orbital on the hydroxylic proton, as in **20**.



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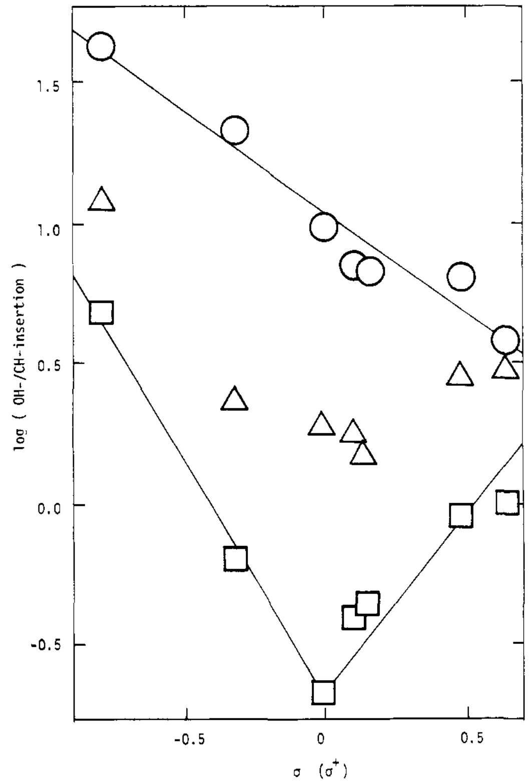
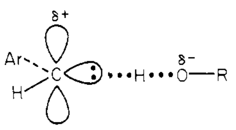


Figure 2. Correlation of product ratios in reaction 3 with Hammett constants: (○) at 20 °C; (□) at −196 °C; (△) at −78 °C.



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Effects of aryl substituents on the insertion selectivities of arylcarbene in *i*-PrOH matrix at -196 °C, summarized in Table III, were somewhat unexpected from those observed at ambient temperature. It is immediately evident that not only electron-donating groups but also electron-withdrawing groups favor OH insertion at this low temperature. A correlation of these ratios with Hammett constants is illustrated in Figure 2. This is not explained in terms of the suggested destabilizing effects of electronegative groups either on singlet carbene (**19**) or on the transition state (**20**) for OH insertion. Similar parabolic deviations from linearity are well documented[34] for reactions in which a change in substituent induces a concomitant change in reaction mechanism. Such deviations are also observed for systems in which the measured rate coefficient is a complex function of several rate and equilibrium constants.[34] If one accepts that all ethereal products are derived from singlet carbene throughout the temperature ranges studied and that the singlet carbene is stabilized by both kinds of substituents through nonbonded interaction, the simplest interpretation of the parabolic deviation in Figure 2 is a variation in the singlet–triplet equilibrium constant as a function of substituents. However, sensitized experiments indicate that reactions of the carbene with alcohol are slower than the singlet–triplet equilibrium. It is important to examine the effects of substituents on the insertion processes of singlet and triplet carbenes. Kinetic studies[19] show that hydrogen-atom abstraction of triplet carbene from the matrix is tunneling in nature. The rate of a hydrogen-atom tunneling process is dependent upon the barrier height and width: the barrier height is the classical activation energy and the barrier width is the distance the hydrogen atom must tunnel.[35a] From the absolute rate decay of arylcarbenes by ESR thus far reported,[19] the order of several triplet carbene reactivities in the matrix can be estimated as follow: monophenylcarbene > fluoroenylidene > diphenylcarbene > naphthylcarbenes > 2-pyrrylcarbene > 9-anthrylcarbene. Unfortunately, the measurement has not been made in terms of ring substituents. Platz and Senthilnathan[19b] have examined the origin of the reactivity difference between naphthyl-, pyrryl-, and anthrylcarbenes. They have suggested that the barrier height will be relatively constant for these carbenes since it is the nonconjugated, in-plane carbene orbital that is abstracting hydrogen, but that the observed reactivity does not fit in with a barrier width estimated from a simple model. This implies that the origin of the relative reactivities may well reside in the microcrystalline environment of the respective carbene. The carbenes are immobilized relative to the host molecules with which they react, and the reactivity in the matrix will depend on its fixed orientation relative to the host. Nonexponential decay of carbenes[19] and marked changes in C–H insertion selectivities[14,24] have been explained by different sites offering various degrees of freedom for reaction in the matrix. It is difficult to reconcile the multiple-site problem with the "V"-shaped correlation of the reactivity with substituents since reactivity is critically dependent on the steric accessibility of the migrating atom rather than the electronic nature of the carbene. A decrease in temperature may also cause a change in the mechanism of OH insertion of singlet carbene, because a similar deviation of the Hammett plot was evident even when the photolysis was carried out at -78 °C (Figure 2). At this temperature, the reaction phase is still liquid where no matrix effects are operating. Since proton-transfer activity of alcohol might decrease with decreasing temperature,[35b] it is very tempting to suppose that, as the interaction of the electron-rich, carbene σ orbital with an electronegative substituent becomes significant, nucleophilicity of the carbene would be reduced and hence nucleophilic attack on proton becomes less favorable especially at lower temperature. Concomitantly, such interaction would increase the electrophilicity of the carbene to the extent that would permit electrophilic ylidic attack of singlet carbene on the oxygen atom of the alcohol with proton rearrangement prevailing. Previous investigations have indicated a delicate balance of both carbonium ion and ylide mechanisms in the reaction of arylcarbenes with alcohols. The fact that photolysis of DPD in a methanolic solution of lithium azide produced benzhydryl methyl ether and azide and that reactivity of alcohols toward DPC generated photolytically increased with increasing acidity of the hydroxy group supported the carbonium mechanism.[11] Nevertheless, studies[12] of isotope effects on the product-forming steps in the thermolysis of DDM in alcohols suggested the ylide mechanism. More recently, Kirmse has shown[11b] that the mechanism of OH insertion depends upon the electrophilic vs. nucleophilic character of the carbene. Thus, cyclopentadienylidene is likely to follow the ylidic mechanism whereas cycloheptatrienylidene might be protonated with formation of the stable tropylium ion. The present study implies that the mechanism can vary not only with structure of carbene but also with the method of generation.

Concluding Remarks

Present results reveal that arylcarbene insertion selectivities into alcohols are highly sensitive to reaction temperature as well as aryl substituents. It should be pointed out that the low-temperature photolytic method is a very useful technique for generating triplet arylcarbenes. This is because most arylcarbenes are usually in rapid equilibrium with the upper-lying singlet states and hence are not populated in the liquid phase to the extent which permits extensive formation of the products even in sensitized experiments. This unique technique is also expected to be equally successful in detecting triplet arylcarbenes in other reaction systems, in which competitive singlet–triplet reactions occur. Investigations of such effects are being studied further in this laboratory, a part of which has been reported[36] recently.

Experimental Section

Instruments. 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 Me_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 using a 4.0 mm × 2.0 m column packed with OV-17 (5%) on 60–80 mesh Diasolid L. Product distributions were determined with a Yanagimoto System 1000 integrator.

Materials. The aryldiazo compounds **1**,[37] **7**,[38] and **15a–h**[30] were prepared according to literature procedures immediately before use. Authentic samples for identification of reaction products were synthesized as follows. Most of ethers (**2**, **8**, and **16a–h**) were conveniently prepared by the Williamson synthesis.[39] Commercially unavailable C–H insertion products were prepared by the reduction of the corresponding carboxylic acid[40] (**10a** and **11b**), imidolactone[41] (**11c**), ketone[42] (**10b**, **18a**, and **18b**), and benzalacetone[43] (**6c**, **18d**, **18e**, and **18f**) and the Grignard reaction[44] (**10c**, **17a**, **17b**, **17d**, **17e**, and **17f**) of the corresponding ketone with MeMgI. Carbomethoxy (**17g** and **18g**) and cyano derivatives (**17h** and **18h**) were prepared by the cyanation and carbonylation of the corresponding bromo derivatives (**17f** and **18f**), respectively. Satisfactory spectroscopic data have been obtained for all authentic compounds.

Commercial alcohols were used used as solvents after purification.

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Photochemical Reactions and Analyses. All irradiations were carried out using a Halos 300-W high-pressure mercury lamp with a water-cooled quartz jacket. In a typical procedure, 0.005 mmol of the diazo compound was added to 2.0 mL of the appropriate alcohol in Pyrex tubes. The sample was then degassed, sealed, and suspended in a transparent Pyrex Dewar filled with coolant. Coolants were water (20 °C), ice–water (~0 °C), dry ice–ethanol (−78 °C), liquid nitrogen–isopentane (−110 and −155 °C), and liquid nitrogen (−196 °C). Irradiation was generally continued until all the diazo compound was destroyed. When irradiation was performed in the solid phase, a second Pyrex tube was inserted into the sample tube in order to maximize exposure and utilization of radiation. The method greatly reduced the irradiation period especially in solid-phase experiments. Since control experiments confirmed that insertion ratios were relatively sensitive to the period of irradiation–thaw cycles, the irradiations outlined in Tables I–III were conducted over 4-h intervals without thawing the matrix in the dark, unless otherwise indicated. Sensitized experiments were performed under conditions similar to those described above. Usually a 50-molar 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 rates of decomposition was noted even in the solid-phase experiment. No products from the reactions of carbene with benzophenone, e.g., oxirane were detected. Control experiments exclude possible photoconversion of the product during the irradiation period and also demonstrate that no reaction occurs in the absence of light over the temperature range studied.

Product identifications were established either by GC as well as GC-MS comparisons using authentic samples synthesized as described above or by isolating individual components followed by spectroscopic identification. Product distributions were conveniently determined by standard GC technique.

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Registry No. 1, 766-91-6; **7**, 883-40-9; **15** (X = *p*-MeO), 23304-25-8; **15** (X = *p*-Me), 23304-24-7; **15** (X = *p*-Cl), 19277-54-4; **15** (X = *m*-MeO), 65864-99-5; **15** (X = *p*-Br), 73900-14-8; **15** (X = *p*-CO_2Me), 73900-18-2; **15** (X = *p*-CN), 70135-28-3; MeOH, 67-56-1; EtOH, 64-17-5; *i*-PrOH, 67-63-0.

Studies of the Tautomerism of Purine and the Protonation of Purine and Its 7- and 9-Methyl Derivatives by Nitrogen-15 Nuclear Magnetic Resonance Spectroscopy[1]

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Abstract: The nitrogen-15 NMR shifts of purine and its 7- and 9-methyl derivatives were measured at the natural-abundance level as a function of pH. The results made it possible for both the sites and magnitudes of protonation of purine and its derivatives to be determined. A semiquantitative determination was made of the position of the N7H–N9H tautomeric equilibria of purine in both water and dimethyl sulfoxide.

Nitrogen-15 NMR has proved very valuable for investigating the protonation of the bases which are components of the nucleic acids, nucleosides, nucleotides, and related compounds.[2,3] Because of the biological importance of nucleic acids, proton magnetic resonance ^{1}H (NMR) has been used extensively to study the stabilization and enzymatic replication of such compounds.[4,5] However, attempts to elucidate the course of protonation of purine by ^{1}H NMR were not conclusive.[6] The additional ambiguity associated with the tautomeric equilibrium of its N7H and N9H forms suggested that ^{15}N NMR spectroscopy might be especially effective for investigating the protonation and tautomeric behavior of the nitrogens of purine.

We describe here the results of an ^{15}N NMR study of purine and its 7-methyl and 9-methyl derivatives in aqueous solution over the pH range 0 to 9. The course of protonation of purine in dimethyl sulfoxide attendant to titration with trifluoroacetic acid was also examined. The results indicate essentially exclusive protonation of purine and its derivatives on the N1 nitrogen.

Table I. Nitrogen-15 Chemical Shifts of Purine and Derivatives[a]

compound	N1	N3	N7	N9
purine	109.7	124.8	181.6	185.7
	(14.3)	(14.0)	(10.3)	(9.1)
purine (dimethyl sulfoxide)	98.4	116.0	166.8	187.3
	(16.5)	(15.2)	(9.7)	(9.7)
9-methylpurine	109.3	132.7	145.0	244.1
	(14.6)	(14.6)	(11.1)	(8.5)
7-methylpurine	108.5	116.7	229.4	143.0
	(13.8)	(13.7)	(9.4)	(11.7)

[a] In ppm upfield from external $D^{15}NO_3$. The spectra were taken in aqueous solution unless otherwise indicated. The $^2J_{^{15}N-H}$ couplings Hz, values (in parentheses) reported here are regarded as being uncertain by at most ±1.5 Hz.

Experimental Section

Purine was commercially available and was used without further purification.

A suspension of purine (10 g, 0.083 mol) and sodium hydride (57%; 0.46 g, 0.083 mol) in *N*,*N*-dimethylformamide (20 ml) was stirred under argon at 0 °C for 20 min. Methyl iodide (11.7 g, 0.083 mol) was added and the resulting mixture was stirred for 2 h. The *N*,*N*-dimethylformamide was removed under reduced pressure, and dry-column chromatography with 95% ethanol afforded 1.66 g (15%) of 7-methylpurine, mp 180 °C (lit.[7] mp 183 °C), and 4.45 g (40%) of 9-methylpurine, mp 160 °C (lit.[7] mp 165 °C). An alternative preparation of 7-methylpurine has

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