

Kinetic Topochemical Effect on Methanol Insertion into Phenyl- α -ketocarbeneDae Dong Sung,^{*} Zoon Ha Ryu,[†] Min-Ho Jeong,[‡] Yong Ho Kim,[§] Ikchoon Lee,[#] and Dinesh, C. Bilehal*Department of Chemistry, Dong-A University, Busan 604-714, Korea. *E-mail: ddsung@dau.ac.kr**†Department of Chemistry, Dong-Eui University, Busan 614-714, Korea**‡Department of Microbiology, Medical School, Dong-A University, Busan 602-714, Korea**§College of Biomedical Science and Engineering, Inje University, Kimhae, Kyongnam 621-749, Korea**#Department of Chemistry, Inha University, Incheon 402-751, Korea**Received June 20, 2008*

The matrix isolation of methanol insertion has been performed into phenyl- α -ketocarbene (PKC) along with temperature decrease from the room temperature to the cryogenic temperature and the critical point of structure-spin inversion has been obtained by the kinetic results. The matrix isolation spectroscopic technique has been employed and the rate constants have been obtained by the laser flash photolysis and FT-IR and UV/vis spectroscopic measurements. The results show that the singlet carbene reacts through a proton abstraction in the high temperature range, 254-312 K, whereas the non-Arrhenius behavior and abnormal temperature effect on the magnitude of the Hammett ρ indicates that the triplet carbene reaction occurs in the low temperature range, 77-154 K. The spin inversion was found to occur at about 254 K. A strong relationship exists between the spin state of the carbene and the geometry and reactivity of the carbene. It was found that the colder matrices of hexafluorobenzene and methanol are more rigid and permits a smaller range of motion for the PKC, and the reaction is controlled by topochemical inversion.

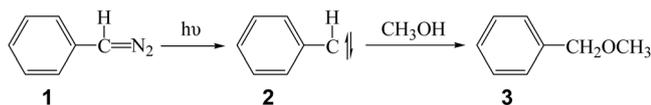
Key Words : Matrix isolation, Topochemical effect, Methanol insertion, Spin inversion

Introduction

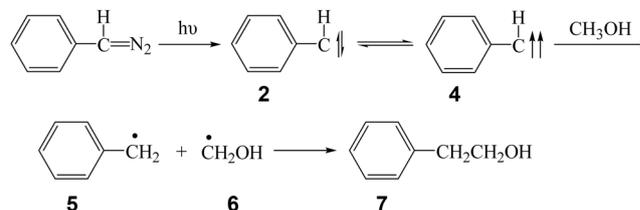
The relationship between reactivity and structure has long been a considerable interest to organic chemists. Generally the organic molecules are more flexible and transformed easily into a kind of metamorphosed structure than inorganic molecules in the solid and liquid¹ phases.

Structural transformation in organic reactions is known to be controlled by temperature and energy. The molecular geometry in organic solid state generally changes differently from those in the liquid state. Geometric control is relatively easy in organic solid state, whereas it is not possible in liquid phase.

An interesting unresolved problem of the difference in the geometric controls in solid relative to liquid state is the methanol insertion into phenylcarbene. An intermediate, phenylcarbene, reacts with methanol to give mainly an O-H insertion product, **3**. It is generally believed that the O-H insertion is a characteristic reaction of singlet carbene, **2**.²



In this reaction, a trace amount of hydrogen abstraction product, **7**, is formed concurrently by a radical pair (**5** and **6**) combination reaction. The radical pair combination in this reaction is generally known to occur by a triplet carbene, **4**, which is produced from the singlet carbene, **2**, by a spin inversion.



In connection with the methanol reaction into phenylcarbene, other O-H insertions of phenylcarbene in ethanol and 2-propanol have also been investigated.³⁻⁷ The yield of the triplet product of phenylcarbene increases with ethanol and 2-propanol and also with cooling of the solution compared to the singlet product of phenylcarbene.

The reaction of phenylcarbene with 2,3-dimethylbutane has been reported to show that the product ratio of tertiary/primary depends on the effect of temperature and matrix according to C-H insertion selectivity. The matrix effect in this case is generally recognized as an example of 'topochemical principle' as enunciated by Schmidt and co-workers.^{8,9}

The yield of C-H insertion products in the methanol insertion into phenylcarbene is increased in solid matrix relative to expectations based on simple extrapolation of the solution phase results.² The tendency of the matrix-isolated radical pairs for phenylcarbene has been observed in olefinic matrices.¹⁰ The effect of matrix and temperature are a matter of primary concern in view of the variety of unique features of the crystalline phase. The solid state of methanol matrix may be expected to give a geometric control that could be determined from the structure of the products in phenyl-

carbene reactions. This geometric control contributes differently in other phases. It seems to reflect that the product ratio in the solid phase relative to that in the liquid phase depends on the relative amounts of the triplet phenylcarbene product to the singlet phenylcarbene product. This phenomenon would be connected with the relationship between geometry and reactivity, and also with other microscopic perturbations. It is thought that the colder matrix is more rigid and permits a smaller range of motion for the reactants. Even though the results of this matrix effect are usually interpreted by this approach, a question arises as to how the matrix effect operates by simply changing the multiplicity of phenylcarbene from singlet to triplet electronic state.

Changing multiplicities of phenylcarbenes and similar aromatic carbenes have been studied based only on the technique of matrix isolation spectroscopy.^{11,12} Although many efforts to find the evidence for critical temperature limit of the phenylcarbene reaction, the results are still not satisfactory in finding out the structure-reactivity relationship through kinetic evidence and with a definite spin multiplicity.

In this paper we examined the matrix isolation of methanol insertion into *p*-substituted phenyl- α -ketocarbene (PKC) carefully according to temperature decrease from the room temperature to the cryogenic temperature, and determined the critical point of structure-spin inversion from kinetic results. For this purpose, we have employed the matrix isolation spectroscopic technique using a laser flash photolysis, and FT-IR and UV/vis spectroscopic measurements were made to obtain rate constants.

Experimental

General Methods. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AC-200 MHz spectrometer for identification of synthesized *p*-substituted phenyl- α -diazoketones (PDK) and the final photolytic reaction products. DEPT and APT proton spin decoupled spectra were obtained on a Bruker AC 500 MHz NMR spectrometer. The chemical shifts are reported in δ (ppm) with tetramethylsilane as internal standard. IR spectra were recorded on a Bruker IF 66 Fourier transform spectrometer interfaced with an OPUS-NT 3D data system. The GC/MS spectrometer was an Hewlett Packard 5890 Series GC system with an HP-ultra-2 (SE-54, 5% phenylmethylsilicon capillary column (50.0 m \times 0.2 mm \times 0.30 μ m)). The gas chromatograph was linked to an HP5973 mass selective detector. UV/vis spectra were recorded on a JASCO V-500 spectrometer. Methanol was purified by distillation from magnesium ribbon and stored under an argon atmosphere. Hexafluorobenzene, 99.5%, NMR grade was purchased from Aldrich and washed four times with distilled water and dried with phosphorus pentoxide, then fractionally crystallized 15 times. The criterion of purity was the melting point, 4.082 ± 0.005 °C, which indicated a purity of $99.993 \pm 0.0005\%$ molality. Other reagents were purchased from commercial sources and used without purification, unless noted otherwise. The substrates,

p-substituted phenyl- α -diazoketones (PDK) were synthesized freshly by the method of the literature.¹³

Laser Flash Photolysis Measurements. Each stock solution of *p*-substituted phenyl- α -diazoketones (PDK) for laser flash photolysis (LFP) measurements was prepared with a proper range of the optical density and placed in a 3 mL cuvette. A Spectron-mode-locked Nd:YAG laser (308 nm, 120 mJ, 10 ns) was used for LFP. LFP measurements at low temperature were performed connected with a R.G. Hansen & Associates P/N 3232 Complete High Tran Cryogenic System at 77 K and 154 K proportional temperature controller to regulate the temperature and were performed in general thermostat for other temperatures at 312 K, 296 K and 254 K. To avoid destruction of the matrix, the laser power was kept on 2.5 W and the beam was defocused to a diameter of 8 mm. Under this condition, disappearance of diazo group was observed at its IR intense band of 2065 cm^{-1} .

Samples for LFP measurements were contained in a Suprasil quartz fluorescence-free static cell for excitation at 308nm. Photochemical kinetics were monitored using a JASCO V-550 UV/vis spectrophotometer and Bruker 500 Fourier-transform infrared spectrophotometer equipped with a Cary sixcell Peltier constant temperature accessory as previously reported.¹⁴⁻²⁰ All samples were deaerated by purging with oxygen-free nitrogen unless otherwise indicated. For kinetic data the observed values at the monitoring wavelength were averaged for each concentration of methanol at least three times. For spectral purpose at least three measurements at each wavelength were averaged. A stock solution of PDK in hexafluorobenzene was injected into an equilibrated methanol for 30 min. and strong absorption peaks corresponding to the singlet carbenes were observed at 271, 274, 276 and 277 nm for *p*-methoxyphenyl- α -diazoketone (*p*-OCH₃), *p*-toluene- α -diazoketone (*p*-CH₃), phenyl- α -diazoketone (*p*-H), and *p*-chlorophenyl- α -diazoketone (*p*-Cl), respectively. LFP of PDK in hexafluorobenzene 1.05 M methanol produces a transient spectrum with an intense, broad band to show a peak at 490-510 nm corresponding to the spectrum of proton abstracted to singlet phenylketocarbene (PKC), *i.e.* a carbenium ion. Low temperature kinetic data were obtained by replacing the normal sample holder with a 10 \times 10 cm brass block fitted with an internal coil which was connected to a liquid nitrogen cryostat equipped with a quartz outer window and sapphire inner window. The temperature was controlled by the boil-off rate control system of nitrogen connected to a resistance heater in the dewar. The temperature was monitored with a thermocouple and was maintained constant to within 0.5 degree. The diazo compound, PDK was dissolved in methanol, placed in a long-necked quartz cuvette of 1-mm path length, and degassed by four freeze-degas-thaw cycles at a pressure near 10^{-5} torr. The cuvette was flame-sealed, under reduced pressure, placed in the cryostat, and cooled to 154 K and finally to 77 K. The sample was irradiated in the spectrometer with a Hanova 500-W high-pressure mercury lamp using a pyrex filter, and the spectral changes were recorded at appropriate time intervals. To find the topochemical point

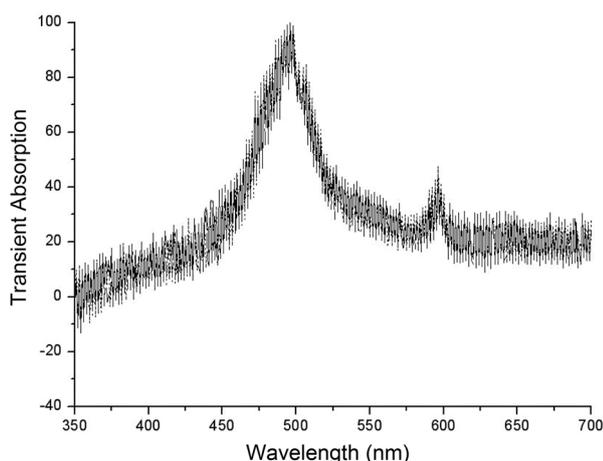


Figure 1. Transient absorption spectrum produced by laser flash photolysis of *p*-methoxyphenyl- α -diazoketone (PDK) in hexafluorobenzene at 312 K.

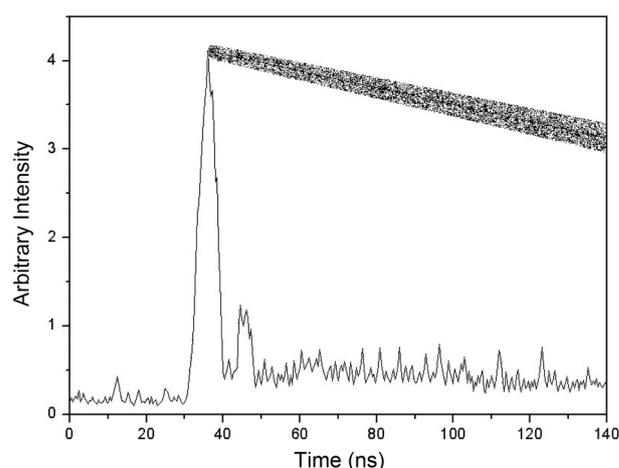


Figure 2. Time resolved fluorescence decay profile corresponding to the forming step of proton abstracted to *p*-methoxy phenyl- α -ketocarbene (PKC) intermediate in hexafluorobenzene at 312 K, monitored at 496 nm.

depending on the temperature, each kinetic run corresponding to the temperature was performed at 77 K, 154 K, 254 K, 296 K and 312 K as the same method as previously mentioned in the liquid nitrogen cryostat increasing the temperature using the thermocouple.¹⁷⁻²⁰

Results and Discussion

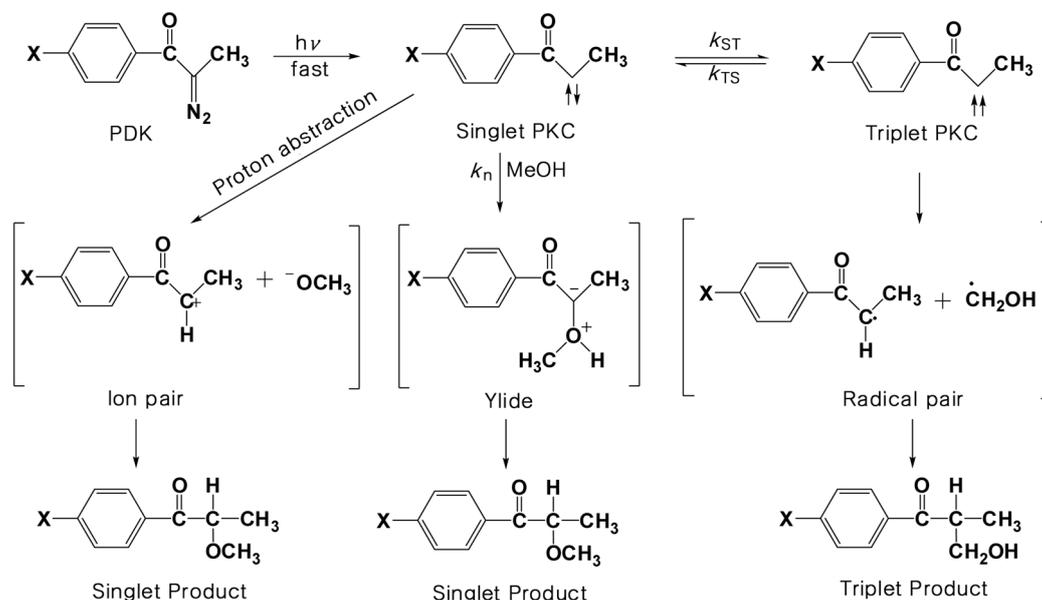
Laser flash photolysis of *p*-methoxyphenyl- α -diazoketone ($X = p\text{-OCH}_3$) in neat under deoxygenated condition of hexafluorobenzene produces a transient spectrum corresponding to the proton abstracted to a singlet phenyl- α -ketocarbene (PKC), *i.e.* a carbenium ion, with a sharp absorption at 496 nm and a shoulder at 599 nm coincided with the weak transient band of *p*-OCH₃ as shown in Figures 1 and 2.

This transient cationic species produced from LFP was

formed in an exponential process that could be analyzed to obtain k_{obs} , the pseudo-first-order rate constant. The value of k_{obs} is linearly dependent on the concentration of methanol. The absolute rate constant k_M was obtained from the slope of this plot as shown in eq. (1),

$$k_{\text{obs}} = k_0 + k_M[\text{MeOH}] \quad (1)$$

where, k_0 is a pseudo-first-order constant for reactions that may undergo in the solvent used, hexafluorobenzene, in the absence of substrates, or for other side reactions. The possibility of the triplet carbene product was confirmed for every PDK reaction with methanol. The methanol was captured only by singlet carbene even though the triplet carbene is equilibrated fast with singlet carbene soon after produced by photodecomposition of PDK as shown in Scheme 1.



Scheme 1

Table 1. Absolute Rate Constants (k_M) and Arrhenius Parameters for the Reaction of *p*-Substituted Phenyl- α -Diazoketone with Methanol in Hexafluorobenzene

substrate, X	temperature	k_M ($M^{-1}s^{-1}$)	E_a^a (kcal/mol)
<i>p</i> -OMe	77 K	$7.78(\pm 0.04) \times 10^6$	–
	154 K	$8.52(\pm 0.06) \times 10^6$	–
	254 K	$1.31(\pm 0.03) \times 10^7$	
	296 K	$2.31(\pm 0.07) \times 10^7$	2.01 ($r = 0.9991$)
	312 K	$2.74(\pm 0.05) \times 10^7$	
<i>p</i> -H	77 K	$7.66(\pm 0.02) \times 10^6$	–
	154 K	$8.17(\pm 0.04) \times 10^6$	–
	254 K	$1.08(\pm 0.07) \times 10^7$	
	296 K	$2.16(\pm 0.03) \times 10^7$	2.45 ($r = 0.9990$)
	312 K	$2.65(\pm 0.06) \times 10^7$	
<i>p</i> -Cl	77 K	$7.50(\pm 0.05) \times 10^6$	–
	154 K	$7.64(\pm 0.04) \times 10^6$	–
	254 K	$8.17(\pm 0.07) \times 10^6$	
	296 K	$1.89(\pm 0.06) \times 10^7$	2.97 ($r = 0.9992$)
	312 K	$2.43(\pm 0.07) \times 10^7$	

^aCalculated using rate constants at only three temperatures, 254 K, 296 K and 312 K, and the maximum errors calculated are ± 0.005 kcal/mol. The rate constants, k_M were averaged more than three kinetic runs and were reproducible to within $\pm 3\%$. ^bThe standard deviations of E_a values were less than 0.01 (with an average value of 0.006) in all cases.

The absolute rate constants, k_M , for all PDK are summarized with Arrhenius parameters in Table 1.

The rate constant, k_M , increases with electron donation by a group substituted in the *para* position of PKC. This is most probably due to an initial attack of the nonbonding electron pair of the carbene carbon of PKC to the positive end, H atom, of the methanol in a proton abstraction process. The methanol insertion reaction into phenylcarbene is well known to give a kind of singlet product as above-mentioned² as through two kind mechanisms; one is ion pair intermediate and the other is ylide intermediate³⁻⁷ as shown in Scheme 1. On the other hand, the radical pair combination occurs partially in the case of triplet carbene which is originally produced from the singlet carbene by a spin inversion.^{6,7} If the reaction is involved the triplet carbene, the reaction occurs through the radical pairs to give a triplet product as shown in Scheme 1.

In this study, the laser flash photolysis of PKC in neat under deoxygenated condition of hexafluorobenzene shows a transient spectrum corresponding to the proton abstracted to a singlet PKC carbenium ion, with a sharp absorption at 496 nm and a shoulder at 599 nm coincided with the weak transient band of *p*-OCH₃ as shown in Figures 1 and 2. This means that the reaction does not occur through the ylide intermediate in Scheme 1. The strong peak at 599 nm found in this reaction corresponds to the transient carbenium ion formed. The resulting carbenium ion and the methoxide anion, ⁻OCH₃, collapses subsequently in Scheme 1. The Hammett plots using k_M values at 254 K (Table 1) gave a negative slope of $\rho = -0.41 \pm 0.06$ ($r = 0.987$) which further supports the carbenium ion formation in a proton abstraction

pathway. The negative sign of ρ precludes the ylide pathway for the singlet carbene, PKC in Scheme 1, since negative charge develops, $\rho > 0$, at the carbene carbon of triplet PKC in forming step of the ylide intermediate. A similar experimental observation for *p*-methoxyphenylcarbene reaction with alkenes has been reported to show a nucleophilic property²¹ of the carbene. Generally the arylcarbene reactions depend not only on the strong nucleophilic properties according to the substituent effect of the arylcarbene but also on the counter reactant including reaction medium.²²

The rate constant decreases considerably in the low temperature range between 154 K and 77 K as shown in Table 1. It seems that the mechanism of methanol insertion into the carbene of the PKC changes when temperature is changed from a high temperature to a low temperature range. The Arrhenius plots show two kinds of slope; one with steep negative slopes in the high temperature region, and the other with much lower slopes in the low temperature range as shown in Figure 3. The Hammett plots also show two different trends; in the high temperature range, the absolute magnitude of ρ decreases with a rise in temperature ($\rho = -0.41, -0.17, \text{ and } -0.10$ at 254, 296, and 312 K, respectively) which is a normal behavior expected for the effect of temperature on a selectivity parameter, whereas in the low temperature range the absolute magnitude of ρ increases ($\rho = -0.03, \text{ and } -0.09$ at 77 and 154 K, respectively) with an increase in temperature which is an inverse of the normal effect of temperature. In the region of high temperature, it was possible to follow the concomitant growth of the carbenium ion formed from a singlet carbene, while we were able to confirm products formed from the radical reaction pathway due to the triplet carbenes in Scheme 1. The mechanistic variation of the transient carbenes can be explained by induction effect of the softening of the matrix between high and low temperature domains.²³

The two groups of Arrhenius plots for high and low temperature regions meet at about 254 K ($ca 4 \times 1000/T [K^{-1}]$) when the two plots are extrapolated as shown in

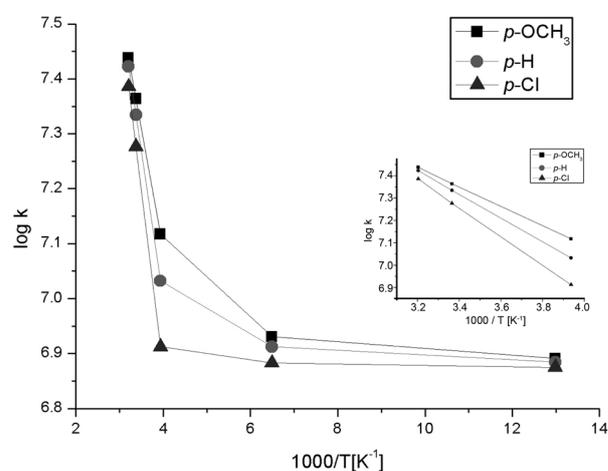
**Figure 3.** Arrhenius plots for the Reaction of *p*-Substituted Phenyl- α -Diazoketones with Methanol in Hexafluorobenzene (inset, plotted between 254 K-312 K).

Figure 3. The meeting point is believed to represent a spin inversion point from singlet to triplet as temperature is lowered. The high negative slope is observed at the point of growing the peak corresponding to the singlet product, while a non-Arrhenius plot is observed at the point of growing the peak corresponding to the triplet product. The non-Arrhenius plots should indicate that the reactions in cryogenic temperatures proceed through triplet carbene intermediate. It is also proposed that the curvature is due to kinetic traps usually observed in the multiphasic kinetics.^{24,25} The rigid matrix in the low temperature suppresses singlet in favor of triplet processes as has been reported by Miller, *et.al.*²⁶⁻³⁰ The migration of a large phenyl group is effectively blocked by the rigid matrix, as it requires a greater range of motion than the matrix can accommodate. It might be shown that the rate of a given bimolecular reaction decreases as the diffusion rate is drastically reduced in the matrix. It is therefore likely that the rate of proton abstraction by a singlet carbene is reduced due to increased viscosity in the low temperature range, which then rises with the elevation of temperature through an isokinetic point at about 254 K. Increasing viscosity in the low temperature range is possible to invert the spin of PKC and it gives a triplet product easily.^{5,31} The simple triplet carbene, diphenylcarbene³² or fluorenylidene carbene^{6,33} can be produced at low temperatures to give radical pairs as very similar to as shown in Scheme 1.

For proving the mechanism change-over on the spin flip, the final product was identified at the low temperature, 77 K by observations of FT-IR and electron paramagnetic resonance (EPR) spectroscopic measurements. A broad and strong band is observed at 3600 cm⁻¹ corresponding to OH group. However the band disappeared increasing the temperature to 254 K. The zero-field splitting (ZFS) parameters, *D* and *E* values are determined by the EPR spectra which are corresponding to the relative distance between electrons with parallel spins. The parameters, *D*-values are shown as 0.4028, 0.4137 and 0.4482 cm⁻¹ for X = Cl, X = H and X = OMe of each PKC respectively. The parameters, *E*-values are also shown as 0.0199, 0.0198 and 0.0196 cm⁻¹ for X = Cl, X = H and X = OMe of each PKC respectively. These values for *D* and *E* are close to the values reported typical triplet carbenes as shown in substituted diphenylcarbene intermediates.³⁴ Therefore the triplet carbene, PKC in this study could be concluded to be related strongly to give a radical pair product and finally to produce the triplet product in the low temperature region as shown in Scheme 1.

The energy difference between the singlet and triplet phenylcarbene (ΔE_{st}) is larger for *p*-substituted phenylcarbene with an electron withdrawing group than that for an electron donating group, as shown as 10.3 kcal/mol for *p*-NO₂ and 4.1 kcal/mol for *p*-CH₃ from the reported calculation.³⁵ This might explain the relatively facile spin inversion found for *p*-OMe substituted carbene in this work.

In conclusion, the singlet carbene reacts through a proton abstraction in the high temperature range, 254-312 K, whereas the non-Arrhenius behavior and abnormal temper-

ature effect on the magnitude of the Hammett ρ indicate that the triplet carbene reaction occurs in the low temperature range, 77-154 K. The spin inversion was found to occur at about 254 K. This shows that there is a strong relationship between the spin state of a carbene and the geometry and reactivity of the carbene. It has been shown that the colder matrices of hexafluorobenzene and methanol are more rigid and permits a smaller range of motion for the PKC, and the reaction is controlled by topochemical inversion.

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