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Kinetic Isotope Effects as Probes of the Mechanism of Reaction of 1-Naphthylcarbene with Cyclohexane and Toluene

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Abstract: The rates of reaction of 1-naphthylcarbene (1-NC) in hydrocarbon solution have been measured with excimer laser flash photolysis of 1-naphthyldiazomethane. The kinetic data were obtained by monitoring the growth of the 1-naphthylmethyl radical (1-NCH) at 370 nm. The observed kinetic deuterium isotope effect for the reaction of 1-NC with cyclohexane (cyclohexane-d_{12}) in 2,2,4-trimethylpentane (k_H/k_D = 1.32 ± 0.17) and the high CH insertion to H-atom abstraction product ratio are consistent with largely singlet reactivity for 1-NC. In toluene, where addition to the aromatic ring is favored over hydrogen atom abstraction, the measured inverse isotope effect (k_H/k_D = 0.52 ± 0.05) also argues for predominantly singlet reactivity and a small singlet–triplet energy gap. The Arrhenius activation parameters measured for the reaction of NC with cyclohexane and toluene were E_{act} = 2.43 ± 0.19 kcal/mol, log (A, s^{-1}) = 7.70 ± 0.15 and E_{act} = 1.93 ± 0.38 kcal/mol, log (A, s^{-1}) = 7.28 + 0.30, respectively.

There have been several reports in the recent literature concerning the effect of spin state multiplicity on the reactions of aryl carbenes.[1] Central issues in these investigations have included determination of the magnitude of the singlet–triplet energy gap (ΔG_{ST}) and the assumption of a singlet–triplet spin state equilibrium.[2] Advances in laser flash photolysis techniques have allowed the direct measurement of the reaction rates of carbenes in the gas phase and in solution.[3] However, while previous experiments have used laser flash photolysis data in conjunction with reactions assumed to be spin state specific in order to measure the singlet–triplet energy gap,[4] the assumption of the state specificity for these reactions has come under criticism.[1a,2c]

The evaluation of kinetic deuterium isotope effects for the C–H insertion and H-atom abstraction reactions of arylcarbenes can provide key mechanistic insights into the spin state reactivities of these carbenes.[5] For example, in a recent study, Scaiano, Platz, and Hadel examined the hydrogen atom abstraction reactions of diphenylcarbene (DPC) in hydrocarbons.[1d] The measured large, primary kinetic deuterium isotope effects in cyclohexane (k_H/k_D = 2.6) and toluene (6.5) were taken as an indication of extensive triplet DPC participation in the overall rates. This is in marked contrast to the results obtained from the reaction of fluorenylidene (FL) with cyclohexane (k_H/k_D = 1.1) where a much smaller singlet–triplet energy gap exists and the singlet state dominates the chemistry.[1e,f]

An analysis of the products obtained from the reaction of aryl carbenes with hydrogen atom donors can also be used as a qualitative indicator of the magnitude of the singlet–triplet energy gap and spin state reactivities. Thus, for example, DPC (large ΔG_{ST}, high triplet reactivity) exhibits extensive hydrogen atom abstraction in cyclohexane[6] whereas FL (small ΔG_{ST}, high singlet reactivity) produces the formal C–H insertion product in high yields under identical conditions.[1e]

Although many reports on the kinetics of the reactions of diarylcarbenes with hydrocarbons exist, the study of monoarylcarbenes has received less attention. This is due, in part, to the fact that the absorption spectrum of phenylcarbene (and substituted phenylcarbenes) strongly overlaps the precursor diazo compound absorption, thus making optical detection of these species experimentally difficult. The chemistry of 1-naphthylcarbene (1-NC), however, has been examined in recent studies by Platz et al.[7,10] This report included data on the flash photolysis of 1-naphthyldiazomethane in hexafluorobenzene, benzene, acetonitrile, and cyclohexane. In the aromatic solvents no observable transients were evident between 350 and 700 nm. In acetonitrile, however, a strong absorption (λ_{max} = 386 nm) was observed with a growth lifetime of 100 ns. This transient absorption was assigned to the corresponding nitrile ylide since its spectral, chemical, and kinetic characteristics were similar to those reported for the ylide resulting from the reaction of fluorenylidene with nitrile solvents. In cyclohexane the only transient species observed in the flash photolysis of 1-naphthyldiazomethane was that of the 1-naphthylmethyl radical (1-NCH) which is formed by hydrogen atom abstraction from the solvent. The growth kinetics of the 1-NCH were measured at its absorption maximum (363 nm) to yield a growth lifetime of 144 ns. The absorption signal due to triplet 1-NC was, however, not observed. It was argued that the 1-NC absorption was sufficiently blue-shifted relative to the corresponding radical that absorption from the 1-naphthyldiazomethane would obscure the signal. Indeed, most triplet carbenes that have been reported to date exhibit absorption

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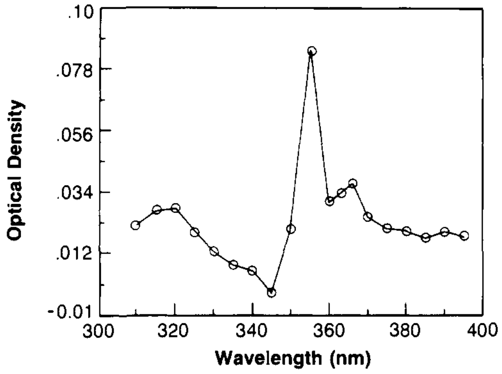


Figure 1. The absorption spectrum obtained 60 ns after 308 nm laser excitation of 1-naphthyldiazomethane in N_2-purged 2,2,4-trimethylpentane.

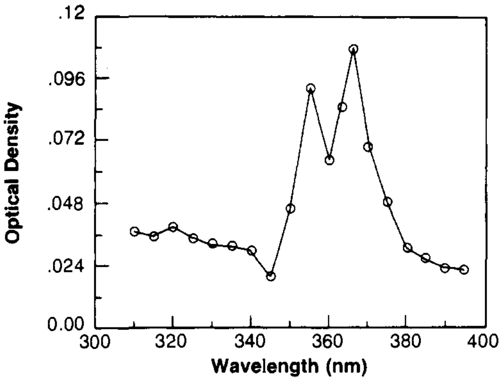


Figure 2. The absorption spectrum recorded 500 ns after 308 nm laser excitation of 1-naphthyldiazomethane in N_2-purged 2,2,4-trimethylpentane.

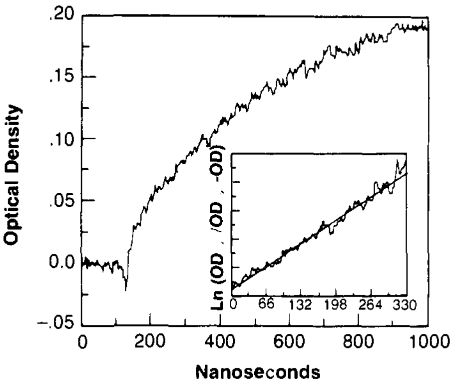
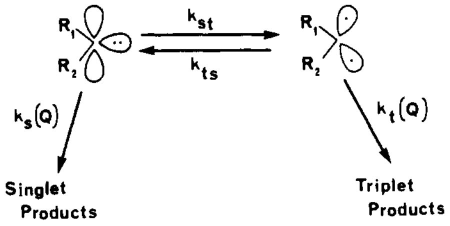


Figure 3. Pseudo-first-order growth of 1-NCH in N_2-purged 2,2,4-trimethylpentane monitored at 370 nm (300 K).

Scheme I. The Singlet–Triplet Equilibrium for the Reaction of Arylcarbenes



For monitoring a triplet pathway :

$$k = k_t + (k_{ts}/k_{st})k_s$$

maxima 20–30 nm blue-shifted relative to the corresponding protio radical.[1,4b,8] The present information concerning the reactions of 1-NC in solution is therefore consistent with a singlet–triplet equilibrium wherein the chemistry of the carbene will be dependent upon the singlet–triplet energy gap and the rates of reaction from each multiplicity.[7,9–11]

The present study was concerned with the characterization of the chemistry of 1-NC by the measurement of the kinetic deuterium isotope effects for its reactions in hydrogen atom donating solvents. In addition, product analyses were employed in order to provide additional information concerning the multiplicity dependent reactivities of 1-NC.

Results and Discussion

Laser Flash Photolysis. The 308 nm excimer laser flash photolysis of 1-naphthyldiazomethane in 2,2,4-trimethylpentane (TMP) produces a transient species absorbing at 355 nm which appears coincident with the laser pulse. Thus the upper limit on the growth lifetime of this species is ca. 2 ns. Shown in Figure 1 is the absorption spectrum obtained 60 ns after laser excitation. At longer time intervals after laser excitation, a transient species with an absorption maximum at 366 nm grows in at the expense of the 355-nm transient (Figure 2). The 366-nm transient exhibits a first-order kinetic growth (τ = 300 ns) as shown in Figure 3. The spectral and kinetic characteristics of the absorption at 366 nm are identical with previous reports of the 1-naphthylmethyl radical (1-NCH).[7,12] The detection of 1-NCH coupling products in cyclohexane (vide infra) and the absence of these products and the 366-nm transient in benzene where H-atom abstraction is unlikely also corroborate this assignment.

The decay of the absorption maximum at 355 nm is kinetically correlated with the growth of the 1-NCH at 366 nm. This transient is therefore assigned as triplet 1-naphthylcarbene (1-NC). Support for this assignment includes the spectral blue-shift relative to 1-NCH, the observation that oxygen, alcohol, and olefins significantly quench the absorption, and the fact that its spectral properties and pattern of reactivity are analogous to those reported for 2-naphthylcarbene.[13] Although triplet 1-NC absorbs strongly at 355 nm, the true absorption maximum of triplet 1-NC is probably at a shorter wavelength than 355 nm where a strong difference spectrum resulting from the ground-state absorption of the precursor 1-naphthyldiazomethane makes detection experimentally difficult.

TMP proved to be one of the most "inert" solvents to 1-NC and was therefore the solvent of choice for all kinetic analyses of the reactions of 1-NC with cyclohexane and toluene. This may be attributed to the high ratio of primary to secondary and tertiary hydrogens in this highly branched hydrocarbon resulting in few sites for facile hydrogen atom abstraction. Consistent with this pattern of reactivity is the fact that detection of 1-NC in *n*-pentane or cyclohexane is difficult or impossible, whereas in these same solvents rapid and facile formation of 1-NCH is observed.

Kinetic Analysis. Since there is substantial spectral overlap between 1-NC and 1-NCH between 350 and 360 nm, the kinetics of the reaction of 1-NC in solution with cyclohexane and toluene were obtained by monitoring the growth of the 1-NCH. At 370 nm the 1-NCH signal is strong and the kinetic growth is found to be cleanly first-order. Thus it is possible to obtain pseudo-first-order rate constants for 1-NC in solution by using this method (vide infra).

The kinetic data obtained from laser flash photolysis studies involving arylcarbenes have been interpreted in terms of a singlet–triplet equilibrium involving the two lowest electronic states available to these species (Scheme I). If the intermediates (singlet and triplet 1-NC) are in equilibrium and react via different

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mechanisms, the product ratios of carbene reactions are assumed to obey the Curtin–Hammett principle, and the kinetics are assumed to follow the Winstein–Holness equation.[14] Thus if one kinetically monitors a purely triplet pathway, the rate constant that is obtained will have a contribution from both multiplicities. For example, if one measures the kinetics of hydrogen atom abstraction from cyclohexane by triplet 1-NC a pseudo-first-order kinetic expression will result as shown in eq 1. However, the

$$-d[1\text{-NC}^3]/dt = k[1\text{-NC}^3] \qquad (1)$$

concentration of 1-NC^3 as a function of time depends upon all modes of reaction of 1-NC. Thus the triplet carbene concentration as a function of time is represented by eq 2 where the second term in the equation represents the hydrogen atom abstraction reaction

$$[1\text{-NC}^3]_t = [1\text{-NC}^3]_0 - [1\text{-NC}^3]_0 e^{(-k_{1\text{-NC}^3})} - [1\text{-NC}^3]_0 e^{(-k_{1\text{-NC}^1}/K_{eq})t} \qquad (2)$$

and the third term represents back intersystem crossing and reaction from the singlet state. Since the growth rate of the radical and the decay rate of the triplet carbene are kinetically correlated, the growth rate of radical can be represented by eq 3. Integration of this equation yields an observed rate constant for the formation of 1-NCH as shown in eq 4. Thus the kinetics observed in laser

$$\frac{d[1\text{-NCH}]}{dt} = \frac{-d[1\text{-NC}^3]}{dt} = (k_{1\text{-NC}^3} + k_{1\text{-NC}^1}/K_{eq})[1\text{-NC}^3] \qquad (3)$$

$$k = k_{1\text{-NC}^3} + \frac{k_{1\text{-NC}^1}}{K_{eq}} \qquad (4)$$

flash photolysis experiments will have contributions from the reaction rates for both spin states and will be dependent upon the singlet–triplet equilibrium constant. Gaspar, however, has recently reported evidence that the addition of styrene or butadiene to fluorenylidene in solution disturbs the singlet–triplet equilibrium.[2a] If a rapid equilibrium is not maintained, a more complex kinetic expression results.[15]

A common method used to obtain bimolecular quenching rates is to set up a competition between the solvent and an added quencher.[3] Thus by adding known amounts of a quencher the rate observed will increase as a function of quencher concentration. In this case, the growth of 1-NCH in TMP can be measured at various concentrations of cyclohexane or toluene. A plot of the observed pseudo-first-order rate constants vs. the quencher concentration should yield the bimolecular quenching rate constant (k_q) as the slope. This analysis will follow 5, where k_{obsd} is the

$$k_{obsd} = k_o + k_q[Q] \qquad Q = \text{quencher} \qquad (5)$$

experimentally observed pseudo-first-order rate constant for 1-NCH growth, k_o is the rate constant observed in the absence of quencher, and k_q is the bimolecular quenching rate constant. The intercept obtained from this analysis (k_o) is thus the pseudo-first-order rate constant in the neat solvent. By using TMP as the solvent in these experiments, the k_o would thus be equal to k'[TMP] where k' includes the bimolecular rate constant for the reaction of 1-NC with TMP and any other first-order modes of carbene decay. It should be noted, however, that eq 5 is linear only if $k_q \gg k_o$ or if the concentration of TMP is constant with respect to the concentration of quencher. For 1-NC in TMP this is not the case since the rate constants for reaction of 1-NC with toluene or cyclohexane are comparable with its rate constant for reaction with TMP. Thus large volumes of quencher are required in order to measure k_q accurately. Therefore, the changes in TMP concentration must be accounted for in the kinetic analysis. Dividing both sides of eq 5 by the concentration of TMP will correct for the decrease in TMP concentration upon the addition of added quencher. This is shown in eq 6. By using eq 6, a plot

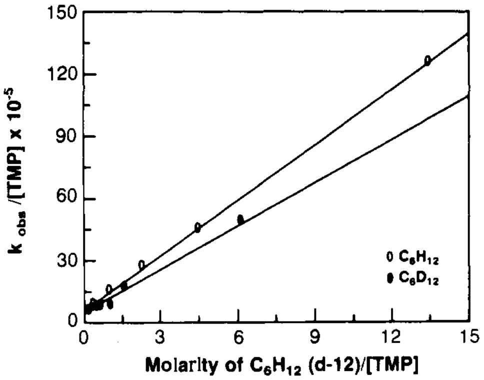
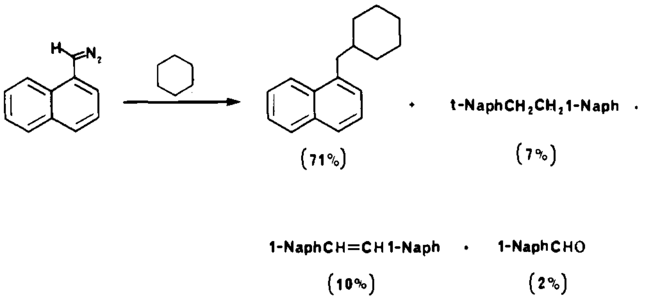


Figure 4. Quenching plots for the reaction of 1-NC with cyclohexane (○) and cyclohexane-d_{12} (●) plotted according to eq 6.

Scheme II. Reaction Products Obtained from the Irradiation of 1-Naphthyldiazomethane in N_2-Purged Cyclohexane



$$\frac{k_{obsd}}{[\text{TMP}]} = k' + k_q\frac{[\text{Q}]}{[\text{TMP}]} \qquad (6)$$

of k_{obsd}/[TMP] vs. [quencher]/[TMP] should afford a straight line with a slope of k_q and an intercept of k' (the rate constant for the reaction of 1-NC with TMP and all catalytic impurities).

Reaction of 1-NC with Cyclohexane. Kinetic analysis of the reaction of 1-NC with cyclohexane according to eq 6 afforded a bimolecular quenching rate constant (k_q) of 8.93 (± 0.11) × 10^5 M^{-1} s^{-1} (Figure 4). This is in agreement with the value obtained for the growth of 1-NCH in neat cyclohexane (calculated growth lifetime from these data is 112 ns as compared to the reported value[7] of 144 ns). The intercept of these data gives a bimolecular rate constant (k') of 6.45 (± 0.28) × 10^5 M^{-1} s^{-1} for the reaction of 1-NC with TMP.

When the same experiment was performed with cyclohexane-d_{12} in lieu of cyclohexane, a lower bimolecular quenching rate constant was obtained as would be expected if hydrogen atom abstraction or C–H bond insertion was a major decay route for 1-NC. Use of the deuteriated material yields a quenching rate constant of 6.75 (± 0.78) × 10^5 M^{-1} s^{-1}. Thus the measured kinetic deuterium isotope effect is 1.32 (± 0.17). The quenching plot for this reaction is also shown in Figure 4. As the concentration of cyclohexane is increased in these experiments, the intensity of the signal due to 1-NCH decreases presumably due to singlet reaction pathways (in this case insertion into the cyclohexane C–H bonds vide infra) which do not produce 1-NCH. This effect is much more pronounced when cyclohexane-d_{12} is used as the quencher. The loss of 1-NCH signal with added cyclohexane-d_{12} agrees with the change in optical density (ΔOD) observed by Platz and Scaiano[10] when comparing the OD of 1-NCH(D) in cyclohexane and cyclohexane-d_{12}. One would expect a substantial kinetic deuterium isotope effect for the H atom abstraction reaction of 1-NC^3 (which produces 1-NCH) in the deuteriated solvent. This results in a proportionally greater involvement of singlet reactivity. The observed small deuterium isotope effect is indicative of extensive

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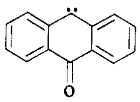
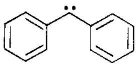
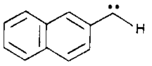
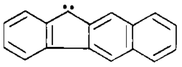
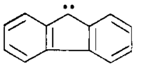
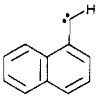
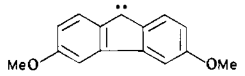
(14) (a) Curtin, D. Y. *Rec. Chem. Prog.* **1954**, *15*, 111. (b) Hammett, L. P. *Physical Organic Chemistry*, 2nd ed.; McGraw-Hill: New York, 1970; p 119. (c) Curtin, D. Y.; Crew, M. C. *J. Am. Chem. Soc.* **1955**, *77*, 354. (d) Eliel, E. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; Vol. 149, p 234.

(15) (a) Seeman, J. I.; Farone, W. A. *J. Org. Chem.* **1978**, *43*, 1854. (b) Zefirov, N. S. *Tetrahedron* **1977**, *33*, 2719.

Table I. Product Distributions for the Reaction of Arylcarbenes with Cyclohexane according to Scheme III

R_1-C-R_2	% I	% II	% III	I/(II + III)	k_H/K_D	ΔG_{ST}, kcal mol^{-1}	ref
	10	44		0.22		>5	18a
	33	32	6	0.85	2.6	5.4^a 3.9^b	1d, 6, 4b
	41	11		3.73	2.6	c	13b
	69	25	6	2.23		<1.0	18d
	65	9	8	3.80	1.2	1.9	1e,f
	71 67	7 3.0	 2.5	9.9 12.2	1.3 2.0	c c	18b 10
	86	2.3	1.6	22.1	1.7	<0	18c

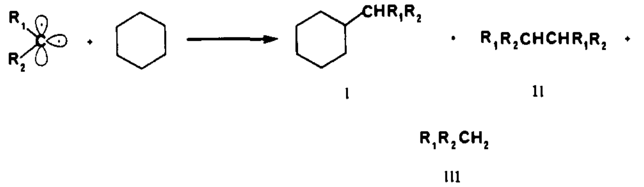
^{a}In isooctane. ^{b}In acetonitrile. ^{c}Not measured, however, ΔG_{ST}(2-NC) > ΔG_{ST}(1-NC).

C–H insertion rather than H atom abstraction by 1-NC in cyclohexane.[1d-f,5,7a] Thus the small primary isotope effect observed for 1-NC in this experiment can be taken as indirect evidence for a rapid singlet–triplet equilibrium in which singlet state reactivity predominates.[16]

Further support for this postulate comes from an analysis of the products which result from the decomposition of 1-naphthyldiazomethane in cyclohexane (Scheme II). Preparative photolysis of 1-naphthyldiazomethane in cyclohexane at room temperture produces a large amount of 1-(cyclohexylmethyl)-naphthalene (71%, the C–H insertion product) in addition to 1,2-di(1-naphthyl)ethane (7.2%, the product formed from the recombination reaction of 1-NCH), 1,2-di(1-naphthyl)ethene (9.7%), and 1-naphthaldehyde (2.3%). The large amount of C–H insertion product compared to radical recombination product indicates extensive singlet reactivity for 1-NC in solution. Although the origin of the 1-(cyclohexylmethyl)naphthalene could alternatively be explained by an abstraction–recombination pathway, this mechanism would be expected to afford a much higher amount of 1,2-di(1-naphthyl)ethane than was observed. Recombination of the benzylic radicals (1-NCH) should be favored over cyclohexyl-1-NCH radical recombination since the cyclohexyl radical is known to disproportionate in solution.[17] A mechanism involving abstraction followed by in-cage recombination can also be eliminated since this should result in a higher isotope effect than that observed.

A generalized reaction product scheme for the reaction of an arylcarbene with cyclohexane is shown in Scheme III. If the assumption is made that product I arises predominantly (though possibly not exclusively) via insertion of the carbene into the C–H bonds of cyclohexane, then the relative amount of product I will directly reflect the extent of participation of singlet carbene in the composite rate law. Likewise, products that originate from single or double hydrogen atom abstraction (products II and III) reflect the relative importance of the triplet carbene. The product distribution in cyclohexane can, therefore, be used as a qualitative indicator of the multiplicity dependent reactivity of an aryl carbene. In light of the large percentage of C–H insertion product formed in the preparative photolysis of 1-naphthyldiazomethane, it is useful to compare these product yields with those from carbenes for which the singlet–triplet energy gap has been determined or estimated. The ratios of singlet product (I) to triplet derived products (II and III) for several aryl carbenes are shown in Table I. As one follows the table from high "triplet" character carbenes (such as anthronylidene and DPC) to high "singlet" character carbenes[19] one can see that the ratio I/(II + III) increases by two orders of magnitude and the kinetic deuterium isotope effect decreases. Therefore, the product study appears to provide a qualitative indication of the magnitude of the singlet–triplet energy gap for arylcarbenes.

Scheme III. Products of the Reaction of Arylcarbenes with Cyclohexane



The kinetic deuterium isotope effect measured by monitoring the 1-NCH growth is a composite of both singlet and triplet 1-NC reactions, if the two carbene spin states are in equilibrium. Therefore the product isotope effect for the singlet 1-NC C–H insertion product 1-(cyclohexylmethyl)naphthalene was also measured. Isolation of 1-(cyclohexylmethyl)naphthalene (product I for 1-NC) in preparative amounts allows for the ^{2}H NMR spectrum to be measured at natural abundance. The ^{2}H NMR spectrum can then be integrated in order to determine the extent of hydrogen vs. deuterium atom transfer to the benzylic position.[20] After statistical correction for the number of reaction sites, a k_H/k_D value is obtained. Measurement of the ^{2}H integral at the benzylic position as compared to the ^{2}H integral for the aliphatic deuterons on the cyclohexane ring in 1-(cyclohexylmethyl)-naphthalene gave a k_H/k_D of 1.7 (± 0.2). In this analysis con-

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(16) This mechanistic argument is analogous to that proposed to explain the reactivity of fluorenylidene. See ref 1e,f. The small ΔG_{ST} observed for 1-NC is most likely a result of the high electron density at the 1-position of naphthalene rather than a compression of the carbene bond angle.

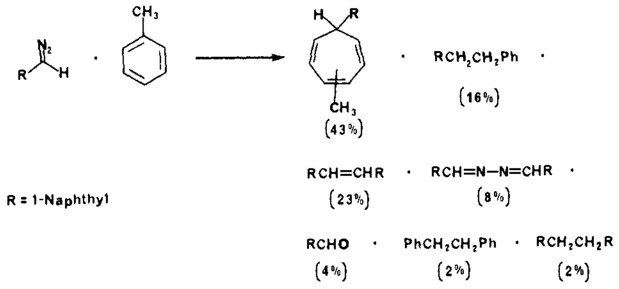
(17) Livant, P.; Lawler, R. G. *J. Am. Chem. Soc.* **1976**, *98*, 6044.

(18) (a) Schuster, G. B. *Aromatic Carbenes: Structure and Reactivity, Advances in Physical Organic Chemistry*, in press. (b) This work. (c) Chuang, C.; Lapin, S. C.; Schrock, A. K.; Schuster, G. B. *J. Am. Chem. Soc.* **1985**, *107*, 4238. (d) Grasse, P. B.; Zupancic, J. J.; Lapin, S. C.; Handrich, M. P.; Schuster, G. B. *J. Org. Chem.* **1985**, *50*, 2352.

(19) The terms "triplet" and "singlet" are meant to refer to the chemically dominant spin state for these carbenes and are not meant to indicate pure spin states or the absence of a singlet–triplet equilibrium.

(20) Pascal, R. A., Jr.; Baum, M. W.; Wagner, C. K.; Rodgers, L. R. *J. Am. Chem. Soc.* **1984**, *106*, 5377.

Scheme IV. Reaction Products Obtained from the Photochemical Decomposition of 1-Naphthyldiazomethane in N_2-Purged Toluene



sideration must be given to the synthetic history of the reactants in terms of natural abundance deuterium content. It was found, for example, that the natural abundance ^2H in the aldehydic position of the 1-naphthaldehyde starting material was enriched by 40% relative to the aromatic positions. Therefore, it was assumed that the aromatic and cyclohexane hydrogen/deuterium ratios were the same and correction made for the enrichment at the benzylic position. This assumption was tested by measuring the ^2H NMR integration of an equimolar mixture of 1-naphthaldehyde and cyclohexane. The integral ratio of the cyclohexyl to naphthyl ^2H was found to be 12:7 within experimental error. In light of these assumptions it is felt that the error in the accuracy of the k_H/k_D value may be greater than the error estimate based upon the precision of the NMR integration. However, the isotope effect measured in this way agrees within experimental error with that obtained by monitoring the growth of the 1-NCH by the flash photolysis technique.

Only a mechanistic picture involving a rapid singlet–triplet 1-NC equilibrium with extensive singlet 1-NC reactivity (C–H insertion) is consistent with the product deuterium isotope effect for C–H insertion being the same as the kinetic deuterium isotope effect for 1-NC decay. Also consistent with this mechanism is the significantly smaller isotope effect measured for the reaction of 1-NC with cyclohexane than measured for the H atom abstraction reactions of diphenyl and other carbenes.

Reaction of 1-NC with Toluene. The preparative photolysis of 1-naphthyldiazomethane in N_2-purged toluene gives the three isomeric 7-(1-naphthyl)methylcycloheptatrienes (43%, Scheme IV) as the major products. Thus the primary reaction pathway involves addition of 1-NC to the aromatic ring of toluene rather than hydrogen atom abstraction. The formation of the 7-(1-naphthyl)methylcycloheptatrienes is most easily rationalized mechanistically by an initial addition of 1-NC to toluene to generate the three isomeric 7-(1-naphthyl)methylnorcaradienes which then undergo a $\pi^4s + \sigma^2s$ electrocyclic ring opening to the corresponding cycloheptatrienes. Thermolysis of 1-naphthyldiazomethane in benzene at reflux has previously been observed to yield 7-(1-naphthyl)cycloheptatriene by a similar rearrangement pathway.[21] The other major 1-NC/toluene product was 1-(1-naphthyl)-2-phenylethane which can arise either from benzylic C–H insertion and/or hydrogen atom abstraction followed by recombination. As noted previously for the reaction with cyclohexane, products which arise from the reaction of 1-NC with 1-naphthyldiazomethane (1,2-di(1-naphthyl)ethene and azine) and oxygen (1-naphthaldehyde) are also produced. Smaller amounts of products assignable to an abstraction–recombination mechanism (1,2-di(1-naphthyl)ethane, 2% and bibenzyl, 2%) are formed. The very small amounts of purely triplet derived products (bibenzyl) and the 1-NCH recombination product 1,2-di(1-naphthylethane) compared to the addition products and insertion product (7-(1-naphthyl)methylcycloheptatrienes and 1-(1-naphthyl)-2-phenylethane) strongly indicate that 1-NC in toluene exhibits a reactivity in which the singlet carbene contributes greatly to the composite rate law. This product study is in contrast with that for DPC in toluene where *no addition* to the aromatic ring is observed[22] and the products are consistent with hydrogen atom abstraction by triplet DPC.

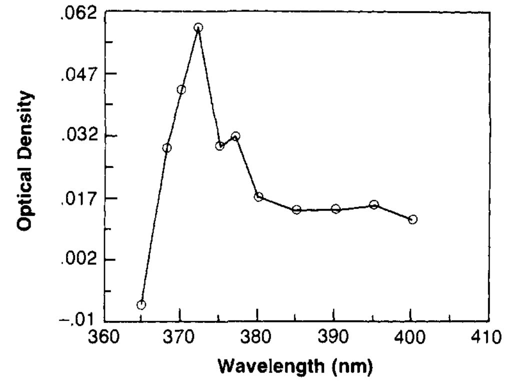


Figure 5. The absorption spectrum obtained 200 ns after the 308 nm laser excitation of 1-naphthyldiazomethane in N_2-purged toluene.

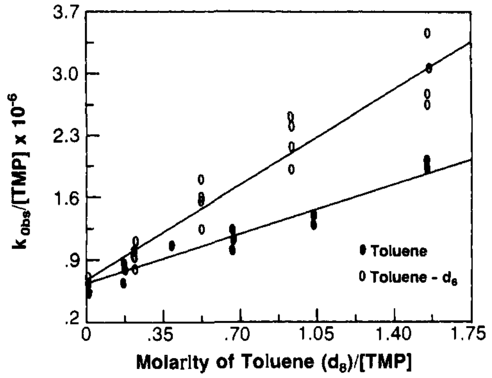


Figure 6. Bimolecular quenching plots according to eq 6 for the reaction of 1-NC with toluene (●) and toluene-d_8 (O) in TMP.

Generation of 1-NC by laser flash photolysis in N_2-purged toluene leads to a transient absorption spectrum somewhat different than that observed in TMP (Figure 5). In the time-resolved spectrum obtained, the 355-nm transient assigned to triplet 1-NC is no longer observed since the 1-naphthyldiazomethane UV spectrum is red-shifted in toluene such that detection of transients below 360 nm is not possible. The 1-NCH radical, however, is seen at 370 nm and this signal increases in intensity with time as was observed in TMP.

Kinetic analysis of the growth of the 1-NCH in TMP with various concentrations of added toluene gave a bimolecular quenching rate constant (k_q) of 7.97 (± 0.34) × 10^5 M^{-1} s^{-1} (Figure 6) at 25 °C. When perdeuterio toluene was used in place of protio toluene, there was a substantial increase in the rate of formation of the 1-NCH ($k_q = 1.54$ (± 0.09) × 10^6 M^{-1} s^{-1}). This leads to an unexpectedly large inverse isotope effect (k_H/k_D = 0.52 ± 0.05) for the reaction of 1-NC with toluene (Figure 6). The inverse isotope effect measured is independent of the batch of 1-naphthyldiazomethane used and the method of purification of the toluene and toluene-d_8.

In these experiments, the loss of the 1-NCH signal with increasing toluene concentration was much more severe than the corresponding loss for the cyclohexane quenching experiments. The use of the deuteriated toluene in lieu of toluene enhanced this problem. This is as expected if a primary kinetic isotope effect for H atom abstraction is operative and addition to the aromatic ring is thereby enhanced. Therefore, relatively low concentrations (less than three molar) of toluene-d_8 were employed to obtain the quenching plots. Although the data for the toluene-d_8 experiments were reproducible within a standard deviation and were found to be unchanged when the toluene-d_8 was rigorously dried and distilled, the error in the measurement of the inverse isotope effect

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(21) Bailey, R. J.; Card, P. J.; Shechter, H. *J. Am. Chem. Soc.* **1983**, *105*, 6096.

(22) Closs, G. L. *Chemically Induced Magnetic Polarization*; Lepley, A. R., Closs, G. L., Eds.; Wiley: New York, 1973; p 101.

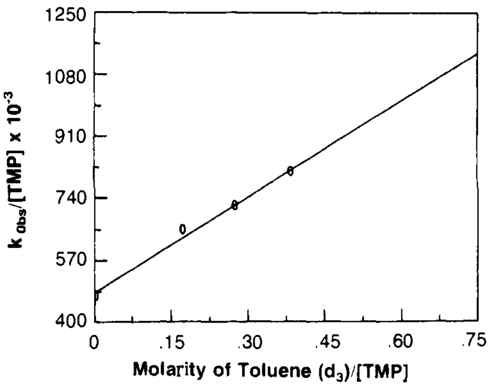

Figure 7. Bimolecular quenching plot according to eq 6 for the reaction of 1-NC with toluene-d_3 in TMP.

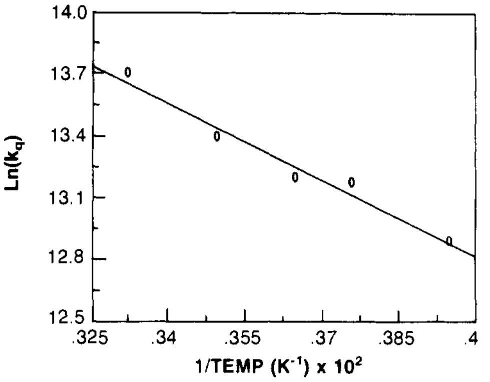

Figure 8. Arrhenius plot for the reaction of 1-NC with cyclohexane.

is probably larger than the standard deviation of the data points.

The existence of an inverse isotope effect is less surprising when one considers that the major products formed are the 7-(1-naphthyl)methylcycloheptatrienes. These products, which require an addition of 1-NC to the toluene π system, potentially require a change in geometry from trigonal planar toward tetrahedral for two of the aromatic ring carbons.[23] Thus the deuterio-substituted compound could be expected to react faster due to the relative differences in zero-point energies for the C–H (D) out-of-plane bending vibrations or CH_2 (HD) twist. Such effects are well-documented for reactions involving geometry changes from sp^2 to sp^3.[24] In order to confirm that this inverse isotope effect is due to the ring deuterons, toluene-d_3 was used in lieu of perdeuterio toluene. The measured kinetic deuterium isotope effect was found to be within one standard deviation of unity, thus showing that the inverse effect observed for toluene-d_8 was indeed due to the sp^2 C–H (D) bonds (Figure 7).

Arrhenius Parameters. The temperature dependencies of the rate constants for 1-NCH growth in both toluene and cyclohexane were also examined. Fitting these rates to an Arrhenius activation parameter plot showed linear behavior over a 48 deg temperature range. The activation energy observed for the reaction of 1-NC with cyclohexane was 2.43 (± 0.19) kcal/mol (log A (s^{-1}) = 7.70 ± 0.15) as shown in Figure 8. In toluene the activation energy is slightly smaller (E_{act} = 1.93 ± 0.38) than for cyclohexane with a similar pre-exponential factor (log A (s^{-1}) = 7.28 ± 0.30).

Although activation energies for carbene reactions have been used in conjunction with flash photolysis data as a test of reaction mechanisms[1a,2c] it is prudent to evaluate these results with caution. If one considers that the observed rate is not a simple rate but a composite rate as described by eq 4, then evaluation of the temperature dependence of k_{obsd} becomes considerably more complex.

Substitution of the temperature dependence of the singlet–triplet equilibrium ($\Delta G_{ST} = -RT \ln K_{ST}$) into eq 4 and rearranging gives eq 7 where A_T, A_S and E_T, E_S are the Arrhenius pre-exponential factors and activation energies for the reactions of triplet and singlet 1-NC, respectively. Thus the slope of a plot of ln k vs.

$$\ln k = \ln (A_T e^{-E_T/RT} e^{-\Delta G/RT} + A_S e^{-E_S/RT}) + \Delta G/RT \quad (7)$$

$1/T$ is a complex function of the singlet–triplet equilibrium constant and the activation energies of all singlet and triplet 1-NC reactions as well as solvent viscosity and volume changes. For the reaction of 1-NC with toluene where the singlet state can partition between addition to the aromatic ring and insertion into the benzylic C–H bonds, the analysis is further complicated. In addition, since the rate of reaction of 1-NC with cyclohexane or toluene is not appreciably larger than that for TMP, there may be an effect from changing the two reaction rates simultaneously in the experiment. If one goes to substantially lower temperatures than those used in these experiments (<–30 °C) the reaction rates of carbenes are known to show complex temperature dependencies. This is particularly true in matrices. Platz has observed this for 1-NC in matrix studies where hydrogen atom tunneling becomes a major reaction pathway.[2,4] Thus although Arrhenius parameters can be useful in the study of carbene reactivity, the complexity of the system should not be ignored and overinterpretation should be avoided.

1-Naphthylcarbene to 2-Naphthylcarbene Comparison. A comparison of the data available on the reactions of 1-NC and 2-NC[13a,b] with hydrocarbons shows that 1-NC exhibits the lower reactivity and the highest singlet character and possesses the smallest singlet–triplet energy gap. Thus, 1-NC reacts at a slower rate with cyclohexane than 2-NC (1-NC $k = 8.8 \times 10^5\ M^{-1}\ s^{-1}$; 2-NC $k = 1.66 \times 10^6\ M^{-1}\ s^{-1}$), yields the smaller isotope effect for reaction with cyclohexane (1-NC k_H/k_D = 1.3; 2-NC k_H/k_D = 2.6), and shows the highest ratio of singlet to triplet reaction products (1-NC I/II + III = 9.9; 2-NC I/II + III = 3.73). Two key molecular structural differences are most likely responsible for the smaller ΔG_{ST} for 1-NC. First, the 1-position of the naphthyl moiety has the largest HOMO orbital coefficient (Hückel 0.425 vs. 0.263) thus leading to the largest stabilization of the carbene center by π–p overlap. Since this would involve a two-electron stabilization for the singlet but only a one-electron net stabilization for the triplet, ΔG_{ST} would be decreased. A second factor potentially contributing to the differences in reactivity between 1-NC and 2-NC is the interaction between the carbene center and the 8-position hydrogen. That this interaction is important is clear from matrix isolation EPR experiments[9,25] that show a preference for the syn conformation of 1-NC. It is also evident that similar 1,8-interactions influence the rate of formation of naphthylmethyl anions and cations.[26]

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(23) Inverse secondary isotope effects have been measured for the addition of a variety of electrophilic reagents to olefins and aromatics.[24] The addition of methyl and trifluoromethyl radicals to ethylene (k_H/k_D = 0.95 and 0.93, respectively), to propene (k_H/k_D = 0.85 and 0.92), and to butadiene (k_H/k_D = 0.83 and 0.92),[24g] the addition of nitronium tetrafluoroborate to toluene (k_H/k_D = 0.85),[24d] and the addition of diphenylketene to styrene (k_H/k_D = 0.93, β position)[24h] all involve addition of the electrophilic reagent to one sp^2 carbon center. The addition of methylene to *cis*-2-butene has also been found to exhibit an inverse secondary isotope effect (k_H/k_D = 0.92).[24i] While a larger isotope effect is expected if two sp^2 centers are involved, the error associated with the measurement of the inverse isotope effect in the present case precludes a quantitative analysis.

(24) (a) Streitweiser, A., Jr.; Jagow, R. H.; Rahey, R. C.; Suzuki, S. *J. Am. Chem. Soc.* **1958**, *80*, 2326. (b) Matsuoka, M.; Szwarc, M. *J. Am. Chem. Soc.* **1961**, *83*, 1260. (c) Denney, D. B.; Tunkel, N. *Chem. Ind.* **1959**, 1383. (d) Olah, G. A.; Kuhn, S. J.; Flood, S. H. *J. Am. Chem. Soc.* **1961**, *83*, 4571. (e) Strausz, O. P.; Safraik, I.; O'Callaghan, W. B.; Gunning, H. E. *J. Am. Chem. Soc.* **1972**, *94*, 1828. (f) Broun, P.; Cookson, R. C. *Tetrahedron* **1965**, *21*, 1993. (g) Feld, M.; Stefani, A. P.; Szwarc, M. *J. Am. Chem. Soc.* **1962**, *84*, 4451. (h) Baldwin, J. E.; Kapecki, J. A. *Ibid.* **1970**, 4874. (i) Simons, J. W.; Rabinovitch, B. S. *Ibid.* **1963**, *85*, 1023.

(25) (a) Senthilnathan, V. P.; Platz, M. S. *J. Am. Chem. Soc.* **1980**, *102*, 7637. (b) Wright, B. B.; Platz, M. S. *Ibid.* **1984**, *106*, 4175. (c) Platz, M. S.; Senthilnathan, V. P.; Wright, B. B.; McCurdy, C. W., Jr. *J. Am. Chem. Soc.* **1982**, *104*, 6494.

(26) (a) Streitweiser, A., Jr.; Longworthy, W. C. *J. Am. Chem. Soc.* **1963**, *85*, 1757. (b) Dewar, M. J. S.; Sampson, R. J. *J. Chem. Soc.* **1956**, 2789. (c) Dewar, M. J. S.; Sampson, R. J. *Ibid.* **1952**, 2946. (d) Dewar, M. J. S.; Dougherty, R. C. *The PMO Theory of Organic Chemistry*; Plenum Press: New York, 1975.

Table II. Kinetic Deuterium Isotope Effects and Arrhenius Activation Parameters for the Reaction of 1-NC with Cyclohexane and Toluene

reactant[a]	K_q (M^{-1} s^{-1})[b,c]	k_H/k_D[c]	E_{act} (kcal/mol)	log A (s^{-1})[d,e]
isooctane	6.45 (± 0.28) × 10^5			
cyclohexane	8.83 (± 0.11) × 10^5		2.43 ± 0.19	7.70 ± 0.15
		1.31 (± 0.17)		
cyclohexane-d_{12}	6.75 (± 0.78) × 10^5			
cyclohexane-d_{12}		1.7 (± 0.2)[f]		
toluene	7.97 (± 0.34) × 10^5		1.93 ± 0.38	7.28 ± 0.30
toluene-d_8	1.54 (± 0.09) × 10^6	0.52 (± 0.05)		
toluene-d_3	8.87 (± 0.97) × 10^5	0.90 (± 0.14)		

[a] [1-Naphthyldiazomethane] = 4.3 × 10^{-4} M in N_2-purged isooctane, λ = 308 nm. [b] Measured by monitoring the growth of 1-NCH at 370 nm. [c] The error limits represent one standard deviation. [d] The activation parameters were measured by monitoring the temperature dependence of k_q. [e] Temperature range from +28 to −20 °C. [f] Measured by natural abundance ^{2}H NMR integration of isolated 1-(cyclohexylmethyl)naphthalene according to the method of ref 20.

Unfortunately, the two effects cannot be isolated with the available experimental data. The low reactivity of 1-NC, however, indirectly points to a stabilized singlet rather than a more reactive sterically crowded carbene center. On the basis of the ability of O, N, and the halogens to stabilize singlet carbenes by π-electron donation and the low barriers to syn–anti isomerization in 1-NC the electron density difference between the 1- and 2-position of the naphthyl HOMO is likely the predominant factor influencing ΔG_{ST} for these two carbenes.

Conclusions

The kinetic and product deuterium isotope data and Arrhenius parameters for the reactions of 1-NC with cyclohexane and toluene are summarized in Table II. The small amount of purely triplet derived products formed in the reactions of 1-NC with cyclohexane and toluene and the small kinetic deuterium isotope effects observed for these systems are consistent with a singlet–triplet 1-NC equilibrium, a small singlet–triplet energy gap, and high singlet 1-NC reactivity. This analysis is in agreement with the original data by Platz et al. on 1-NC in solution[7,10] and the decrease in 1-NCH signal intensity at high concentrations of quencher due to a favoring of singlet reaction pathways. The apparent smaller singlet–triplet energy gap for 1-NC than for 2-naphthylcarbene[13a] appears to be consistent with greater singlet carbene stabilization (π–p overlap) due to the higher electron density in the 1-position of the naphthyl moiety HOMO.

Experimental Section

General. Melting points were obtained on a Buchi circulating oil melting point apparatus and are uncorrected. NMR spectra were recorded either on a Bruker AM 300 (300 MHz) or on a Varian EM-360L (60 MHz, ^{1}H data only) spectrometer. All ^{1}H chemical shifts are reported relative to Me_4Si as an internal standard. All ^{2}H chemical shifts are reported relative to natural abundance ^{2}H in $CHCl_3$ or C_6H_6 as noted. Infrared (IR) spectra were recorded on a Perkin-Elmer 727-B scanning spectrophotometer. Low-resolution mass spectra were taken with a Hewlett Packard Model 5985 mass spectrometer. All spectrophotometric grades of Aldrich Gold Label solvents were distilled over calcium hydride under nitrogen before use unless otherwise noted. Toluene was washed with concentrated H_2SO_4, $NaHCO_3$ (aq), and water before drying over $MgSO_4$ and distillation from lithium aluminum hydride under nitrogen. 1-Naphthyldiazomethane was prepared as described in the literature[11] and was purified by vacuum sublimation at 25 °C and 0.05 Torr over 4 h. The sublimed diazo compound was used immediately after purification. The 1-naphthyldiazomethane purified in this manner melted at 50.5–52.0 °C with decomposition. Toluene-d_8 and cyclohexene-d_{12} were purchased from Stohler-KOR (ICN Biomedicals, Inc.) and were of greater than 99.5% isotopic purity (atom %). Toluene-d_3 was prepared by the method of Renaud et al.[27] and was greater than 90% d_3. All deuteriated solvents were distilled from lithium aluminum hydride prior to use.

Laser Flash Photolysis. The laser flash photolysis apparatus has been described previously.[13a] The excitation source for the laser flash photolyses is a Quanta Ray EXC-1 excimer laser which produces 4 ns fwhm pulses of up to 20 mJ at 308 nm. The transient absorption signals are digitized by a Tektronix 7912AD transient digitizer and then transferred to a Hewlett Packard 9816 computer which provides data processing, storage, and hard copy graphics capabilities. For all of the flash photolysis investigations, the samples of 1-naphthyldiazomethane were contained in 10 × 10 mm (3 mL) quartz fluorescence cuvettes which were fitted with a stopcock for introduction of the sample and N_2 purging. All samples were deaerated by purging with oxygen-free nitrogen unless otherwise indicated.

For kinetic data a minimum of four traces at the monitoring wavelength were averaged for each concentration of quencher. For spectral purposes at least three traces at each wavelength were averaged. Data acquisition for spectra was limited to eight data points per sample to maintain the loss of optical density due to depletion of sample to less than 5%.

Low-temperature traces were obtained by replacing the normal sample holder with a 10 × 10 cm brass block fitted with an internal coil which was connected to a liquid nitrogen dewar. The nitrogen boil off rate, and thereby the temperature, was controlled by varying the current supplied to a resistance heater in the dewar. The temperature was monitored with a thermocouple and was maintained constant to within 1 deg.

Photolysis of 1-Naphthyldiazomethane in Cyclohexane. A solution of 142.3 mg (0.85 mmols) of 1-naphthyldiazomethane in 100 mL of cyclohexane was irradiated for 2 h through Pyrex at ambient temperature. Removal of the solvent in vacuo afforded 164.2 mg of a yellow oil. Chromatographic separation of this material (MPLC, silica gel, hexanes) allowed the separation of three fractions. The first fraction (135.1 mg, 0.60 mmol, 71%) was found to consist of 1-(cyclohexylmethyl)-naphthalene, which agreed in all respects with the spectral and physical data in the literature for this material.[12] The second fraction (22.1 mg) was found to be a mixture of 1,2-di(1-naphthyl)ethane[28] and 1,2-di(1-naphthyl)ethene[11,29] in a ratio of 1:1.6 as determined by ^{1}H NMR integration. The last fraction was identified as 1-naphthaldehyde (3.0 mg, .02 mmol, 2.3%), which exhibited spectral and physical properties identical with those of an authentic sample.

Photolysis of 1-Naphthyldiazomethane in Toluene. An 8.2 mM solution of 1-naphthyldiazomethane (137.48 mg of 1-naphthyldiazomethane in 100 mL of solvent) in toluene under nitrogen was irradiated through Pyrex for 2 h. Concentration in vacuo gave 177.0 mg of a yellow oil. Chromatography on silica gel (eluant hexanes) gave three fractions. The first fraction (86.8 mg) was found to consist of bibenzyl and the three isomeric 7-(1-naphthyl)methylcycloheptatrienes in a 5:95 ratio based on the ^{1}H NMR integration of the bibenzyl CH_2 and the combined methyl peaks of the 7-(1-naphthyl)methylcycloheptatrienes, respectively. Extensive chromatography of this fraction (silica gel, hexanes) separated the bibenzyl from the isomeric 7-(1-naphthyl)methylcycloheptatrienes. Two ^{1}H 2-D COSY (200 MHz) experiments on fractions one enriched with and one depleted of the methyl-7-(1-naphthyl)cycloheptatriene isomer allowed the ^{1}H assignments for all three isomers to be made. Methyl-7-(1-naphthyl)cycloheptatriene (200 MHz, $CDCl_3$) δ 1.50 (s, 3 H), 3.60 (d, 1 H), 6.03 (d of d, 1 H), 6.24 (d, 1 H), 6.35 (d of d, 1 H), 6.68 (d of d, 1 H), 6.70 (d of d, 1 H), 7.2–8.0 (m, 7 H); 2-methyl-7-(1-naphthyl)cycloheptatriene δ 1.98 (s, 3 H), 3.43 (t, 1 H), 5.24 (d, 1 H), 5.6 (m, 1 H), 6.2 (m, 1 H), 6.2 (m, 1 H), 6.65, 6.65, 7.2–8.0 (m, 7 H); 3-methyl-7-(1-naphthyl)cycloheptatriene δ 2.18 (s, 3 H), 3.51 (t, 1 H), 5.52 (m, 1 H), 5.57 (m, 1 H), 6.13 (d, 1 H), 6.2 (m, 1 H), 6.57 (d, 1 H), 7.2–8.0 (m, 7 H). The second fraction (36.8 mg) consisted of a mixture of 2-phenyl-1-(1-naphthyl)ethane[30] and 1,2-di(1-naphthyl)ethene in an 84:16 ratio. The last fraction (37.9 mg) obtained after elution with methylene chloride consisted of 1,2-di(1-naphthyl)ethane, 1-naphthaldazine, 1-naphthaldehyde, and 1,2-di(naphthyl)ethene in a ratio of 7:23:23:47 as determined by ^{1}H NMR integration.

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Registry No. D_2, 7782-39-0; 1-naphthyldiazomethane, 10378-55-9; cyclohexane, 110-82-7; toluene, 108-88-3; 1-naphthylcarbene, 4399-95-5; 4-methyl-7-(1-naphthyl)cycloheptatriene, 108834-96-4; 3-methyl-7-(1-naphthyl)cycloheptatriene, 108834-97-5; 2-methyl-7-(1-naphthyl)cycloheptatriene, 108834-98-6.

Primary and Secondary Kinetic Deuterium Isotope Effects and Transition-State Structures for Benzylic Chlorination and Bromination of Toluene

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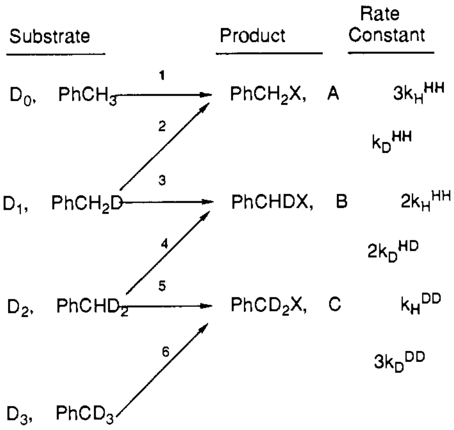
Abstract: As a chemical model for benzylic hydroxylations effected by cytochrome P-450 enzymes, the chlorination of $PhCH_3$, $PhCH_2D$, $PhCHD_2$, and $PhCD_3$ in a two-phase system of hypochlorite/CH_2Cl_2 with a phase-transfer catalyst has been investigated. On the basis of the deuterium content of the product benzyl chlorides, *relative* rate constants were deduced for all possible H- and D-abstractions with these substrates. From this the primary (P) and secondary (S) KDIEs were found to be 5.90 ± 0.41 and 1.03 ± 0.02, respectively, and the "rule of the geometric mean" was found to be closely obeyed. For the analogous bromination of toluene by *N*-bromosuccinimide in CCl_4, P and S were 6.37 ± 0.43 and 1.05 ± 0.01. The transition states of these processes must therefore involve extensive C–H bond breaking but relatively little rehybridization toward planarity at the reacting carbon.

Cytochrome P-450 is a family of mixed function oxidase enzymes that play vital roles in the biotransformation of both endogenous and xenobiotic compounds. Several types of oxygenations of organic substrates are known to be affected, depending on the structure and reactivity of the substrate. Among them aliphatic hydroxylation is particularly interesting to chemists because of the conspicuous lack of chemical reagents for effecting this transformation smoothly with molecular oxygen as the oxidant. Current hypotheses concerning the mechanism of P-450 catalyzed aliphatic hydroxylation envision two major stages.[1,2] The first involves "activation" of O_2 by reductive cleavage to form one molecule of water and an oxoheme or ferryl group. This process is thought to be common to all oxygenations catalyzed by P-450. In the case of *aliphatic* hydroxylation, the second is thought to involve a hydrogen abstraction/hydroxyl recombination step with a transient (caged) radical intermediate.

We have been interested in exploring the mechanism of P-450 catalyzed oxygenation processes through the use of "probe" substrates that either possess unusual electronic structures[3-5] or are substituted with deuterium.[6,7] Recently we examined the P-450 catalyzed benzylic hydroxylation of toluene-*7-d*$_1$ and toluene-*7,7-d*$_2$ to benzyl alcohol.[8] A set of model equations was devised to deconvolute the product isotope content data into values for the primary and secondary kinetic deuterium isotope effects (KDIEs) for this particular hydroxylation. Although the data showed strong preference for abstraction of hydrogen over deuterium, the model equations failed to deconvolute the data in the manner intended. However, the model *did* appear to work satisfactorily when applied to isotope discrimination data for the *chemical chlorination* of the same two deuteriated toluenes. In this case it yielded a primary KDIE of 5.0, but surprisingly, the value calculated for the secondary KDIE was 0.85, i.e., *inverse* rather than normal as might have been expected. Several possible explanations for this result were considered but none were satisfactory.

Scheme I



In the present work we have refined our model equations so that they now take into account inter- as well as intramolecular isotope effects, and we have re-examined the chlorination of the entire series of toluenes $PhCH_nD_{3-n}$ (n = 0–3). Our new model (Scheme I) is found to accommodate all our data to a high degree of precision. It allows us to determine relative rate constants for all six possible H or D abstractions from the various toluenes. For this reaction the effects of deuterium substitution are seen to obey the rule of the geometric mean quite closely. The values for *P* and *S*, the primary and secondary KDIEs, are found to be 5.90 ± 0.41 and 1.034 ± 0.019, respectively, and the reason for the *apparent* inverse secondary KDIE from the earlier model has been identified. The values of *S* and *P* for the bromination of toluene with *N*-bromosuccinimide are not significantly different from those

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