

A Simple Test for Diffusion-Limited Reactions. Near-Diffusion-Controlled Nitrene Insertion into C-H Bonds

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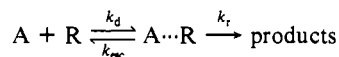
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Abstract: A test for diffusion-controlled reactions is described. It is based on a simple experiment, wherein a reactive intermediate competes for two reagents containing a different number of reactive sites. This approach allows one to estimate rate constants of rapid reactions (i.e., $k_r \approx k_d$) without absolute rate measurements. The test is applied to reactions of (diethoxyphosphoryl)nitrene with hydrocarbons in perfluorinated solvents. The photogenerated singlet nitrene undergoes efficient insertion into C-H bonds, and its reactivity is unaffected by the presence of oxygen. The insertion of the nitrene into a tertiary C-H bond is found to be near-diffusion-controlled with $k_{\text{obs}} \approx 0.3k_{\text{dif}} = 3 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$. Increased selectivity for insertion into tertiary versus primary C-H bonds is observed in perfluorohexane (9.7) as compared to a hydrocarbon solvent (5.7). This diminished reactivity of the nitrene is considered as evidence for complex formation between the singlet nitrene and a solvent molecule. The rate of the complexed-singlet to triplet intersystem crossing is estimated to be $8 \times 10^8 \text{ s}^{-1}$. The triplet nitrene reacts by hydrogen abstraction and is scavenged by oxygen.

Kinetic data for reactive intermediates are not always available from direct measurements due to experimental difficulties. This statement especially applies to transient species without a convenient spectroscopic handle. In solution, the problems are compounded by interference from diffusive processes.¹ Due to the limited mobility of molecules in the condensed phase, reacting partners collide hundreds of times before separating.¹ This phenomenon, known as the cage effect,^{1,2} has received a lot of attention, but the experimental studies have been limited to radical-coupling reactions.^{1,2}

Diffusion-controlled or "in-cage" processes are often invoked to explain unusual reactivities or selectivities of reactive intermediates. Also, many reaction rates are estimated from competition between a first-order process and a second-order reaction, wherein the latter is assumed to be diffusion-limited. A simple experiment to test for diffusion-controlled processes would, therefore, be valuable.

From a phenomenological point of view, an irreversible reaction between reactive solutes A and R in an inert solvent proceeds in two stages: (1) the diffusion of A and R from a large separation to a contact distance, and (2) the subsequent reaction of A and R when in this encounter complex:



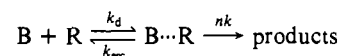
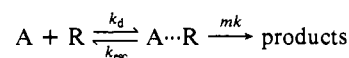
The overall rate coefficient for the formation of products, assuming a steady-state concentration of the encounter pair ($A \cdots R$), is $k_r k_d / (k_r + k_{\text{esc}})$. When the reaction rate is large ($k_r \gg k_{\text{esc}}$), diffusion of the reactants is the limiting process.³ However, if $k_r \approx k_{\text{esc}}$, the overall process is controlled by both diffusion and chemical reaction. For such reactive intermediates, the probability of reaction in the encounter complex will be determined by the relative rates of the two processes. The apparent rate constant (k_{obs}) is then a fraction ($f_c = k_r / (k_r + k_{\text{esc}})$) of the diffusion rate constant, k_d . If known, the ratio of $k_r / k_{\text{esc}} = z$ would be a convenient, quantitative measure of the cage effect.

This article describes a simple test for diffusion-limited reactions, which does not require measurements of absolute rates. The test allows one to determine whether the reaction in question is

diffusion-limited or not, and in cases where the rate of the chemical step is comparable to that of diffusion, it may give estimates of the absolute rate constant for the reaction. The test uses diffusive processes as internal clocks for rapid chemical processes. It is based on two reagents competing for a reactive intermediate and, without any elaborate equipment, yields values of z and, therefore, probabilities of the reaction in the encounter complex.

Results and Discussion

Kinetic Model. Consider a competition experiment between two reagents, A and B, containing m and n reactive sites, respectively. It is assumed that reactive sites are *independent and chemically equivalent*. Within the encounter complex, R reacts with A or B with a rate constant k per active site:



The approach of A and B to R and separation of the resulting encounter complex into its constituents are governed only by the diffusive properties of the reacting molecules. However, in the encounter complex, B will react n/m times as fast as A for statistical reasons. Therefore, as shown⁴ in Appendix A of the supplementary material,

$$\frac{\ln([A]_0/[A])}{\ln([B]_0/[B])} = L = \frac{m k_d^A k_{\text{esc}}^B + nk}{n k_d^B k_{\text{esc}}^A + mk} \quad (1)$$

$$L = \frac{m}{n} \frac{1 + nk/k_{\text{esc}}}{1 + mk/k_{\text{esc}}} \quad (2)$$

For a particularly simple case, where the diffusion coefficients of A and B are equal ($D_A \approx D_B$), this relationship simplifies to eq 2, from which k/k_{esc} (and f_c) can be obtained via the determination of L from competition experiments. A and B could be selected in such a way as to satisfy this condition precisely or approximately. If $D_A \neq D_B$, but the relevant D_i 's could be measured experimentally or calculated, then $k_d^A/k_d^B = k_{\text{esc}}^A/k_{\text{esc}}^B = (D_A + D_R)/(D_B + D_R)$.

If $L = 1$, i.e., both substrates react with the same rate, the reaction is diffusion-limited ($k \gg k_{\text{esc}}$). If $L = m/n$, the reaction rate constant is not comparable to the diffusion rate constant ($k_{\text{esc}} \gg k$). Additionally, for values of L between 1.00 and m/n , the

(1) For a review see: Rice, S. A. Diffusion-Limited Reactions. In *Chemical Kinetics*; Bamford, C. H., Tipper, C. F. H., Compton, R. G., Eds.; Elsevier; New York, 1985; Vol. 25.

(2) Koenig, T.; Fischer, H. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. I, p 157.

(3) In the other extreme, when the reaction rate is small ($k_r \ll k_{\text{esc}}$), the apparent rate constant (k_{obs}) is approximately equal to the intrinsic rate constant ($k_{\text{in}} = k_r k_d / k_{\text{esc}}$).

(4) A steady-state concentration of the encounter complexes is assumed.

Table I. Reaction of (Diethoxyphosphoryl)nitrene with Hydrocarbons **2** and **3**

entry	atm ^a	initial concn, M			% conv ^b	yields based on azide, %						products ratios					
		azide × 10 ³	2	3		9	4	5	6	7 + 8^d	total	P _s ^c /P _T	5/4	(7 + 8)/6	6/4	(6/4)(2/3)	
1	Ar	3.2	7.68		90	40.1	28.2	30.6				1.47	1.08				
2	Ar	3.2		6.88	88	41.0			16.1	42.0	99	1.41		2.61			
3	Ar	3.2	3.64	3.46	39	36.3	14.6	15.3	6.7	17.5	90	1.49	1.05	2.61	0.46	0.48	
4	Ar	3.2	3.84	3.46	88	35.3	14.4	15.1	6.8	17.8	89	1.53	1.05	2.62	0.47	0.52	
5	Ar	3.2	6.54	3.47	85	35.8	18.8	19.6	4.9	12.9	92	1.57	1.04	2.63	0.26	0.49	
6	Ar	3.2	3.84	6.30	81	39.1	10.8	11.4	9.4	24.4	95	1.43	1.06	2.60	0.87	0.53	
7	O ₂	2.2	7.68		43	6.3	29.3	31.6			67	9.7	1.08				
8	O ₂	2.2		6.88	37	3.3			15.6	41.4	60	17.3		2.65			
9	O ₂	2.2	3.84	3.46	31	9.9	10.2	10.6	5.0	12.8	48	3.9	1.04	2.56	0.49	0.54	
												1.06 ± 0.02	2.61 ± 0.03	0.51 ± 0.02			

^aAr = the reaction mixture was deoxygenated and run under argon. O₂ = the reaction mixture was saturated with O₂. ^b% conv = percent of the azide consumed. ^cRatio of singlet products (**4** + **5** + **6** + **7** + **8**) to triplet product (**9**). ^dRatio of **7** to **8** was 0.67 ± 0.05.

reaction is near-diffusion-limited and k/k_{esc} can be determined, and therefore, the reaction rate constants in the range (0.1–0.9) k_d could be conveniently estimated in this way.

In the simplest and most precise version of this test,⁵ reactions of two reagents containing only one kind of equivalent site are followed. However, this approach may be extended to reactions of molecules containing other, chemically nonequivalent, sites (Appendix A of the supplementary material). In such a case, it is necessary to measure the relative amounts of products formed from all nonequivalent sites of A and B. The most convenient way to perform this test is to follow the development of the products at low conversions of A and B.

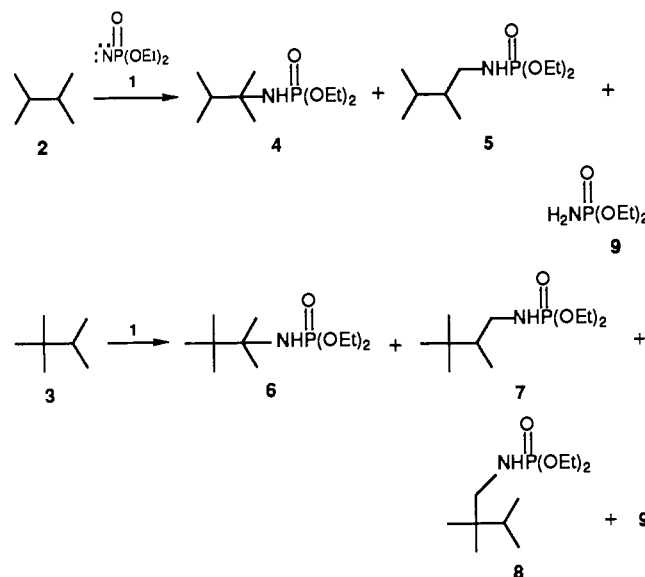
A general equation for reagents A and B containing multiple nonequivalent sites and competing for reagent R is as follows (Appendix A of the supplementary material):

$$\frac{[P_1^A][B]_0}{[P_1^B][A]_0} = \text{ES} = \frac{m}{n} \frac{1 + nz + nz \sum_i [P_i^B]/[P_1^B]}{1 + mz + mz \sum_j [P_j^A]/[P_1^A]} \quad (3)$$

where $z = k_1/k_{\text{esc}}$ and k_1 is the rate constant (per site) of the reaction within the encounter complex leading to product P_1^A or P_1^B . The value of $z/(1+z)$ is a measure of the reaction probability within the encounter complex. Therefore, z is an excellent gauge of the cage effect.

In this model, A contains m equivalent reactive sites of interest, leading to product P_1^A , and j other types of nonequivalent sites,⁶ leading to products P_j^A . Similarly, B has n equivalent sites of interest, giving upon reaction with R product P_1^B , and i other types of nonequivalent sites,⁶ producing P_i^B . The sites of interest in A and B are chemically equivalent and independent of all other sites and each other. The summation is over all i and j sites of B and A, respectively. $[P_1^A][B]_0/[P_1^B][A]_0$ corresponds to *statistically uncorrected intermolecular selectivity* (ES) between chemically equivalent sites of A and B. Correspondingly, $[P_1^A]/[P_1^A]$ and $[P_1^B]/[P_1^B]$ represent *statistically uncorrected intramolecular selectivity* (IS) between different, chemically nonequivalent, sites within A and B. In this model, A and B have identical diffusive properties.

Reactions of Phosphorylnitrene. This test has now been applied to the reaction of (diethoxyphosphoryl)nitrene, **1** (Scheme I). Breslow et al. have reported⁷ that **1** inserts efficiently into C–H bonds with one of the lowest selectivities ever reported for a nitrene. This observation is indicative of a highly ferocious species capable of reacting with diffusion-limited rate. In fact, it has been suggested⁸ that such a highly reactive intermediate can be captured on almost every collision. Surprisingly, mechanistic information about the phosphorylnitrenes is scarce.^{7,8}

Scheme I

Two small hydrocarbons, **2** and **3**, were selected for their similar diffusive properties.⁹ As required by the test, the chosen hydrocarbons differ in the number of C–H insertion sites: 2,3-dimethylbutane has 2 tertiary and 12 primary hydrogens; 2,2,3-trimethylbutane has 1 tertiary and 15 primary hydrogens. Reactions of ferocious intermediates are characterized by very early transition states. For the insertion reaction with such an early transition state, any small electronic and steric differences between tertiary hydrogens in **2** and **3** are believed to be negligible. It is, therefore, assumed that the rate constants (per bond) for insertion into these tertiary C–H bonds within the encounter complex are identical for both hydrocarbons.

To identify the products and verify some of the assumptions discussed above, **1** was first produced in the hydrocarbon solvent by photolysis of diethyl phosphorazidate.^{8,10} However, the actual competition reactions had to be run in an inert solvent. Perfluorohexane, selected because of its reported¹¹ unreactivity toward methylene, proved to be a good choice.

(a) **Reactions in Hydrocarbon Solvent.** When **1** was produced in an excess of deoxygenated **2** or **3**, a clean reaction occurred, giving C–H insertion products phosphoryl amides **4–8** in good yield (Scheme I). Additionally, in both cases, reduction product **9** was observed. The yields of **4–8** were undiminished in reaction mixtures saturated with oxygen, but those of **9** were significantly reduced (Table I). Formation of **9** was also almost completely

(5) This conclusion is based on the error propagation analysis.

(6) Number of reactive sites of various types is irrelevant.

(7) Breslow, R.; Feiring, A.; Herman, F. *J. Am. Chem. Soc.* **1974**, *96*, 5937. See also: (a) Reichle, W. T. *Inorg. Chem.* **1964**, *3*, 402. (b) Harger, M. J. P. *Chem. Commun.* **1971**, 442. (c) Zwierzak, A.; Zawadzki, S. *Tetrahedron* **1973**, *29*, 3899.

(8) Breslow, R.; Herman, F.; Schwabacher, A. W. *J. Am. Chem. Soc.* **1984**, *106*, 5359.

(9) The diffusion coefficients of **2** and **3** in perfluorohexane are identical, as determined from NMR measurements. For the technique see: Hall, L. D.; Luck, S. D. *Carbohydr. Res.* **1984**, *134*, C1. I am indebted to Dr. A. J. Benesi for these measurements.

(10) Scott, F. S.; Riordan, R.; Morton, P. D. *J. Org. Chem.* **1962**, *27*, 4255.

(11) Turro, N. J.; Cha, Y.; Gould, I. R. *J. Am. Chem. Soc.* **1987**, *109*, 2101.

Table II. Reactions of (Diethoxyphosphoryl)nitrene with 2 and 3 in Perfluorohexane

entry	atm ^a	initial concn × 10 ³ , M			% conv ^b	yields based on azide, %						products ratios											
		azide	2	3		9	4	5	6	7 + 8 ^f	total	P _S ^d /P _T	5/4	(7 + 8)/6	6/4	(6/4)(2/3)							
10	Ar	2.60			30	4.0																	
11	O ₂	2.22			48	0.4																	
12	Ar	2.75	37.2		85	30.3	5.2	2.9				38	0.27	0.56									
13	Ar	2.53	37.2		28	18.0	3.8	2.0				24	0.32	0.53									
14	Ar	2.22	74.5		43	30.7	8.9	5.6				45	0.47	0.62									
15	O ₂	2.22	74.5		35	1.2	6.9	4.3				12	9.3	0.63									
16	Ar	2.27		34.1	81	29.0			3.6	5.5		38	0.31		1.53								
17	Ar	2.30		34.1	45	9.2			2.9	4.5		21	0.33		1.55								
18	Ar	2.22		68.2	32	37.4			7.7	11.8		57	0.52		1.53								
19	O ₂	2.22		68.2	33	1.7			6.4	10.6		19	10.0		1.65								
20	Ar	2.27	37.2	34.1	32	31.7	4.3	2.6	2.2	3.9	4.5	45	0.41	0.60	1.77		0.50	0.55					
21 ^e	Ar	2.27	37.2	34.1	92	38.2	5.3	3.3	2.7	4.2	5.4	54	0.40	0.62	1.55		0.51	0.57					
22 ^e	Ar	2.27	23.8	86.6	83	33.5	3.1	1.9	6.6	10.2	5.5	55	0.65	0.61	1.54		2.11	0.58					
23	Ar	2.27	40.6	62.0	86	30.1	4.7	2.7	4.4	6.4	4.8	48	0.60	0.59	1.48		0.93	0.60					
24	Ar	2.27	37.2	41.3	98	40.7	5.0	3.3	3.4	4.5	5.7	57	0.39	0.66	1.33		0.68	0.61					
25 ^e	Ar	2.27	89.4	21.8	88	37.8	11.4	6.9	1.6	2.5	6.0	60	0.59	0.61	1.56		0.14	0.57					
26	Ar	2.27	89.4	81.8	92	25.2	7.4	4.7	3.4	5.6	4.6	46	0.84	0.63	1.61		0.47	0.51					
27 ^e	Ar	2.22	74.5	68.2	44	29.8	7.9	4.8	4.1	6.3	5.3	53	0.78	0.61	1.54		0.51	0.56					
28	O ₂	2.22	74.5	68.2	37	1.5	7.7	4.8	4.2	6.5	2.5	25	15.5	0.62	1.57		0.54	0.59					
29	Ar	2.27	124.2	113.7	45	21.1	6.8	4.0	3.7	6.3	4.2	42	0.99	0.60	1.72		0.54	0.59					
30	Ar	2.22	149.0	136.4	40	24.7	10.4	6.6	5.8	8.9	5.6	56	1.28	0.64	1.54		0.55	0.60					
31	O ₂	2.22	149.0	136.4	36	2.1	11.6	7.2	6.1	9.4	3.6	36	16.3	0.62	1.54		0.52	0.57					
32	Ar	2.22	198.7	181.9	60	34.5	17.7	10.7	9.5	14.6	8.7	87	1.52	0.60	1.54		0.53	0.58					
															0.61 ± 0.03	1.56 ± 0.09			0.58 ± 0.03				

^aAr = the reaction mixture was deoxygenated and run under Argon. O₂ = the reaction mixture was saturated with O₂. ^b% conv ≡ percent of the azide consumed. ^cIn addition, in all runs, small amounts of a compound tentatively identified as a dimer of 1 were detected. This dimer was also produced in reactions run without hydrocarbons (entries 10 and 11). Additionally, small amounts of two unidentified products, one derived from 2 and one from 3, were observed (<10% of the least-abundant amide). These products were absent in reactions run under O₂. ^dRatio of singlet products (4 + 5 + 6 + 7 + 8) to triplet product (9). ^eAverage of six or seven determinations (see text). ^fRatio of 7 to 8 was 0.67 ± 0.05.

inhibited by 1–3% (v/v) isoprene.

Similar results were obtained when the reaction was run in the mixture of 2 and 3. In all these reactions, the ratios of 6 to 4 and (7 + 8) to 5 were within experimental error¹² of those statistically predicted (0.51 (2) versus 0.5 and 1.28 (6) versus 1.25, respectively) after corrections for the hydrocarbon abundance. Additionally, the observed selectivity between primary and tertiary hydrogens was the same for 2 ($k_1/k_3 = 0.177$ (3)) and 3 (0.174 (2)) and was similar to that reported earlier⁷ for 2-methylbutane (0.167). This selectivity was unaffected by the presence of oxygen. The experimental data for these reactions are collected in Table I.

(b) Reactions in Perfluorohexane. In competition experiments, the concentration of hydrocarbons was kept in the 0.04–0.38 M range. The azide concentrations were 2.2–3.3 mM. The molarity of neat C₆F₁₄ is 4.94. Under these conditions, a hydrocarbon molecule is completely surrounded by the solvent molecules (statistically). This situation minimizes reactions between 1 and the hydrocarbon molecule(s) contained in the cage "walls". Such reactions contribute a nondiffusional component to the escape process. The selected ratio of reagents also assures that the hydrocarbon consumption during the experiment is negligible (<5%). The products observed in perfluorohexane (Table II) were identical with those observed in the hydrocarbon solvent. Similarly, oxygen had no effect on the production of 4–8 but dramatically diminished the yield of 9 from the typical 30% to less than 2%.

Generally, in reactions run in perfluorohexane, the total yield of 1–9 was 35–60%. It was observed to be higher in reactions run at higher concentration of the hydrocarbons, reaching almost 90% at the limits of hydrocarbon solubility (Tables II and III). It is important to note, however, from Tables I–III that for reactions in the hydrocarbon solvent as well as in the perfluorinated solvent *the ratios of products were independent of the mass balance, the hydrocarbon concentration, and the degree of azide conversion.* Reaction runs with different relative amounts of 2 and 3 gave experimentally indistinguishable results. To illustrate these points, the average values with standard deviations are listed for appropriate columns in Tables I and II. Similarly to the

Table III. Reaction of (Diethoxyphosphoryl)nitrene with 2 in Perfluorohexane. Effects of Hydrocarbon Concentration on Product Ratios^a

entry	initial 2 concn × 10 ³ , M	% conv ^b	yields based on azide, %				product ratios	
			9	4	5	total	P _S ^c /P _T	5/4
33	38	52	25.4	4.8	3.0	33	0.30	0.63
34	114	51	20.6	9.7	6.0	36	0.75	0.62
35	228	60	20.8	14.2	8.8	44	1.11	0.62
36	304	56	22.0	17.9	11.0	51	1.32	0.61
37	380	49	25.4	23.7	14.8	64	1.52	0.62
38	456	52	21.6	23.7	14.9	60	1.78	0.63
39	523	52	27.9	29.6	18.3	76	1.72	0.62
40	608 ^d	49	28.7	37.0	22.6	88	2.08	0.61

^aAll reactions run under argon atmosphere under identical illumination. Initial concentration of the azide was 2.6 × 10⁻³ M. ^b% conv ≡ percent of the azide consumed. ^cRatio of singlet products (4 + 5) to the triplet-derived product (9). ^dSolubility limit for the hydrocarbon.

situation observed in the hydrocarbon solvent, the insertion selectivity (k_1/k_3) in perfluorohexane was the same for 2 (0.102 (5)) and 3 (0.104 (8)).

(c) Additional Mechanistic Studies. The relative photoefficiencies of the reactions were tested on a photochemical merry-go-round. The azide consumption was used to monitor the reaction progress. The data are included in Tables II and III. All runs included in Table III were obtained in a single experiment to assure identical light intensity for all samples. The concentration of the hydrocarbon had no significant effect on the degree of azide conversion (Table III). The effect of oxygen on the rate of consumption of the azide was tested in pairs of runs (entries 14–15, 18–19, 27–28, and 30–31, Table II). The reproducibly slightly lower conversion of the azide under an oxygen atmosphere than under argon is consistent with some quenching of the singlet azide by O₂ prior to nitrogen loss.¹³

The stereochemistry of insertion was tested with *cis*- and *trans*-1,2-dimethylcyclohexanes¹⁴ (*cis*-10 and *trans*-10). In

(12) Standard deviations of the least significant digits are reported in parentheses throughout the paper. For example, 0.51 (2) = 0.51 ± 0.02.

(13) It is well established that oxygen quenches singlet (and triplet) excited states with diffusion (or near-diffusion) limited rates. See: Turro, N. J. In *Modern Molecular Photochemistry*; The Benjamin/Cummings Publishing Co., Inc.; Menlo Park, CA, 1978; p 589.

perfluorohexane and neat hydrocarbons, the *cis* and *trans* isomers each gave a single tertiary C–H insertion product. These diastereomeric products were easily separated by the capillary GC. The insertion reaction is, therefore, fully stereospecific. It is presumed to occur with retention of configuration.^{14–16}

The isotope effect of the insertion reaction in perfluorohexane was measured with cyclohexane-*1,1,2,2,3,3*-*d*₆ and with mixtures of cyclohexane and cyclohexane-*d*₁₂. These experiments yielded k_h/k_d ratios of 1.14 (3) and 1.02 (3), respectively.

Mechanistic Considerations. In summary, under argon, yields of insertion products **4–8** and reduction product **9** are excellent in the hydrocarbon solvent and moderate to very good in perfluorohexane.¹⁷ Under oxygen, **4–8** are produced in undiminished yields and with selectivity identical with that observed in reactions under argon. Product **9** is found in very small amounts only, probably due to incomplete efficiency of trapping by oxygen.

These data require involvement of at least two reactive intermediates: one trappable by oxygen (or isoprene) and leading to **9**, and one unaffected by oxygen and leading to insertion products **4–8**. The high stereospecificity of the insertion is inconsistent with the radical mechanism¹⁸ for the formation of **4–8**. Based on these data and other published evidence¹⁹ concerning the reactivity of nitrenes, it can be safely concluded that insertion products are formed by direct insertion of the singlet nitrene into the C–H bonds of the hydrocarbons.

The reduction product **9** is most likely derived from the triplet nitrene. The oxygen (or isoprene) trapping reactions may involve the triplet nitrene itself or a radical derived from it upon hydrogen abstraction. It may also be concluded that this radical does not efficiently couple with the alkyl radicals.²⁰ This conclusion is based on the high stereospecificity of the formation of the tertiary C–H-derived amides in the cases of *cis*- and *trans*-**10**, as well as on the identical selectivity (k_1/k_3) of insertion into **2** and **3** under argon and oxygen, since it is quite unlikely that the nitrogen-centered radical will have selectivity identical with that of the singlet nitrene.

Further evidence supporting the involvement of the triplet nitrene will be discussed below. It suffices to state here, however, that the formation of **9** (and **4–8**) by radical-chain processes sometimes observable in azide reactions²¹ is inconsistent with the observed (almost) undiminished photoefficiencies of the azide decomposition and identical selectivities under oxygen and argon. Oxygen would be expected to efficiently quench any chain reactions. For similar reasons, involvement of the excited triplet state azide in the reaction is unlikely¹³ (see below).

Kinetic Analysis of the Insertion Reaction of the Singlet Nitrene. As discussed above, the obtained results are consistent with the singlet-triplet nitrene reactivity and inconsistent with other proposed mechanisms for such reactions.¹⁹ In addition, the literature¹⁹ provides clear evidence that indicates that singlet nitrenes insert into C–H bonds and triplet nitrenes follow radicaloid pathways such as atom transfers. Thus, the yields of the insertion products obtained from the competition experiments in perfluorohexane can be used to evaluate the kinetics of the intermediate involved. According to the evidence presented, this intermediate is the singlet nitrene. It has to be stressed, however, that the following analysis is independent of the actual identity of the intermediate responsible for the insertion products.

The hydrocarbons under study contain multiple nonequivalent reactive sites. Taking into account that insertion selectivity (k_1/k_3)

is, within experimental error, the same for **2** and **3**, eq 3 can be modified appropriately. For the insertion of **1** into a tertiary C–H bond, it can be shown that

$$\frac{[\mathbf{6}][\mathbf{2}]_0}{[\mathbf{4}][\mathbf{3}]_0} = \text{ES} = 0.5 \frac{1 + 2z + 12Sz}{1 + z + 15Sz} \quad (4)$$

where $S = k_1/k_3$, $z = k_3/k_{\text{esc}}$, and k_1 and k_3 are the rate constants for insertion of **1** into a primary and a tertiary C–H bond within the encounter complex, respectively.

This expression assumes that k_3 's are the same for both hydrocarbons, as discussed above. The assumption finds experimental support in the fact that the observed selectivities for **2** and **3** are experimentally indistinguishable (see above). Additional support is provided by the small isotope effect observed for insertion into secondary C–H bonds. This measurement confirms an early transition state for this reaction. As argued previously, the insertion should be, therefore, insensitive to any small steric and electronic differences between **2** and **3**.

For all reactions of **1** in C₆F₁₄, it was found that $([\mathbf{7}] + [\mathbf{8}])/[\mathbf{6}] = 1.56$ (12) and $[\mathbf{5}]/[\mathbf{4}] = 0.61$ (3), which—after statistical correction—gives selectivity between primary and tertiary C–H bonds (k_1/k_3) of 0.103 (6). From the observed averaged ES value of 0.58 (3), the ratio of $k_3/k_{\text{esc}} = z = 0.6$ (4) can be calculated. A more precise estimate may be obtained using only the data from runs 21, 22, 25, and 27 (Table II). These experiments correspond to optimal conditions for the competition²² and were analyzed by multiple GC injections. This limited but more precise set of data yields a z value of 0.4 (1). From these numbers, it can be deduced that, on average, two to four encounters between **1** and a compound containing one tertiary C–H bond are needed before the reaction occurs, i.e., the reaction takes place with ca. 30–40% of the diffusion-limited rate. From the viscosity data,²³ the diffusion rate constant in perfluorohexane at 25 °C is estimated to be $1.0 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$. The k_3^{obs} for the singlet nitrene insertion into a tertiary C–H bond can, therefore, be estimated to be ca. $3 (2) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$.

This estimate assumes that the k_{esc} has purely diffusional character. It has to be kept in mind, however, that nondiffusional contributions to this rate are possible. The reaction of the reactive intermediate with the hydrocarbon molecules contained in the cage walls has been minimized by the appropriate selection of hydrocarbon concentrations. Other nondiffusional contributions to k_{esc} include the intersystem crossing (k_{IC}) of the singlet nitrene to the triplet and the reaction of the singlet nitrene with the "inert" solvent. Both of these cannot be very significant, however. As shown below, k_{IC} is rather small. The good yields of nonfluorinated amides under conditions of high excess of solvent over the hydrocarbon must also signify that the reaction of **1** with perfluorohexane is slow. All these side reactions lead to a slight overestimation of k_{esc} and underestimation of the absolute rate of reaction.

An independent confirmation of the near-diffusion-limited kinetics of C–H insertion may be obtained from the comparison of "intramolecular" and "intermolecular" isotope effects measured for cyclohexane. For reactions much slower than diffusion, both isotope effects should be identical. For reactions much faster than diffusion, the intermolecular isotope effect has to be unity.²⁴ A reduction in the magnitude of the isotope effect between the intramolecular and intermolecular measurements, as observed in this case, signifies a diffusion-limited or near-diffusion-limited reaction. This method may in fact serve as an alternative test for diffusion-limited reactions.²⁵

Singlet-Triplet Intersystem Crossing. Additional evidence

(14) (a) Anastassiou, A. G.; Simmons, H. E. *J. Am. Chem. Soc.* **1967**, *89*, 3177. (b) Anastassiou, A. G. *J. Am. Chem. Soc.* **1967**, *89*, 3184.

(15) Hamlin, K. E.; Freifelder, M. *J. Am. Chem. Soc.* **1953**, *75*, 369.

(16) Compare for example: (a) Simon, J. M.; Lwowski, W. *J. Am. Chem. Soc.* **1969**, *91*, 5107. (b) Inagaki, M.; Shingaki, T.; Nagai, T. *Chem. Lett.* **1981**, 1419.

(17) Compare Table II, footnote c.

(18) It has been shown¹⁵ that the 1,2-dimethylcyclohexyl radical does not react in a stereospecific manner.

(19) For a review see: *Azides and Nitrenes*; Scriven, E. F. Ed.; Academic Press: New York, 1984.

(20) These radicals may undergo disproportionation.

(21) For a summary see ref 19, p 219.

(22) These runs are characterized by good yields of products obtained at relatively low concentrations of hydrocarbons. For these runs $[\text{ES}] = 0.570$ (8) and $[\text{S}] = 0.1026$ (9).

(23) Brice, T. J.; Coon, R. I. *J. Am. Chem. Soc.* **1953**, *75*, 2921.

(24) The intramolecular isotope effect may be equal 1.00 for some ferocious intermediates.

(25) (a) Maslak, P.; Szczepanski, J. J.; Minard, R. D. Manuscript in preparation. (b) Also compare: McBride, J. M. *J. Am. Chem. Soc.* **1971**, *93*, 6302.

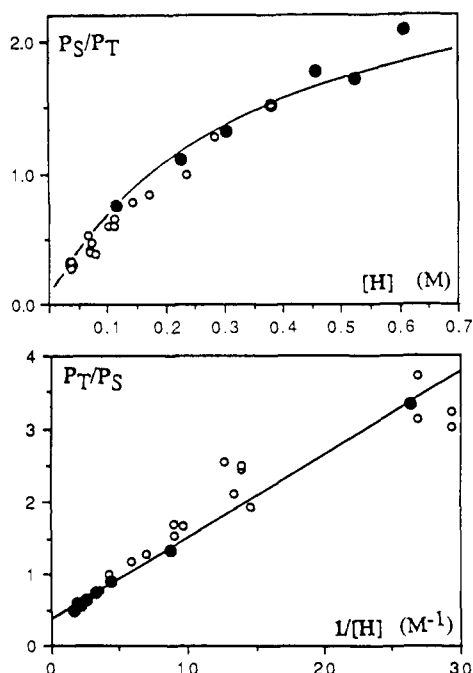


Figure 1. (a, top) Ratio of the singlet products ($P_S = 4-8$) to triplet product ($P_T = 9$) plotted as a function of hydrocarbon concentration. The line represents the correlation of b. (b, bottom) P_T/P_S ratio plotted as a function of the total hydrocarbon concentration. The intercept of this plot (r) equals the singlet azide/triplet azide ratio produced by direct photolysis of the azide. The slope of the line equals $(r + 1)k_{1C}/k_i$. The total absolute rate constant for reaction of **1** with **2** and **3** (k_i) is taken here as equal to k_d . The filled circles represent data obtained from experiments carried out under conditions of identical light intensity (Table III).

supporting the triplet nitrene as the intermediate leading to **9** comes from the insertion/reduction product ratios. It has been argued above that insertion and reduction products are derived from different intermediates. For reactions run in perfluorohexane, the (4-8)/**9** ratio should be independent of the hydrocarbon concentration if the two intermediates involved are singlet nitrene and triplet azide. These intermediates are derived from a common precursor, singlet azide, via a reaction that does not have to involve collisions with a hydrocarbon molecule. The insertion/reduction product ratio would be a linear function of the hydrocarbon concentration if the two intermediates involved were the singlet and triplet nitrene.²⁶ In this case, a common intermediate reacts with a rate that is first-order in the hydrocarbon (insertion), in competition with a process that is essentially zero-order in the hydrocarbon (intersystem crossing).

The experimental data are, however, more complex. A strong but apparently nonlinear dependence of the insertion/reduction product ratios on the hydrocarbon concentration ($[H]$) is observed (Figure 1a). Additionally, a linear extrapolation of the data leads to a nonzero intercept²⁷ (see below). These trends are especially evident for data obtained under conditions of identical light intensity (Table III; filled circles in Figure 1a). These observations exclude the involvement of the triplet azide as the major intermediate responsible for the formation of **9** and leave us with a mechanism in which the insertion and reduction products are derived from the singlet and triplet nitrenes, respectively.

To account for the observed curvature in the plot (Figure 1a), some of the triplet nitrene must be derived from an intermediate other than the singlet nitrene. It is quite likely that this alternative pathway involves interconversion of the singlet azide to the triplet azide before the loss of nitrogen. Taking into account that the

triplet azide itself is an unlikely²⁸ source of **9** (see above), a kinetic analysis of such a scheme (Appendix B of the supplementary material) indicates that the plot of the ratio of triplet (P_T) to singlet (P_S) products versus $1/[H]$ should yield a line with the intercept equal to the singlet azide/triplet azide ratio (r) obtained by direct photolysis. This ratio reflects the relative rates of nitrogen loss from the singlet azide and its intersystem crossing to the triplet azide. The data plotted according to this analysis are shown in Figure 1b. An excellent linear correlation ($P_T/P_S = 0.35(2) + 0.114(2)/[H]$; $r^2 = 0.999$) observed for the experiments run under identical illumination (Table III; filled circles in Figure 1b) strongly supports this mechanism. Some scatter observed for other data points may be attributed to changes in light intensity in various experiments and use of **2** and **3** in the reaction mixture.

A reversible intersystem crossing, however, may also account for the observed trend²⁷ (Figure 1a). This alternative would require that the curvature be due to the experimental scatter, most likely in the low concentration range. In fact, if all points are included in the analysis, both graphical presentations describe the data equally well. The alternatives could be tested by populating the triplet azide via triplet sensitization with acetophenone. Unfortunately, the energy transfer from the triplet acetophenone to diethyl phosphorazidate is very inefficient. Only low conversion of the azide was observed upon prolonged irradiation of the sensitizer ($\lambda > 300$ nm). Nevertheless, the reduction product **9** was clearly present, and no insertion products were detected. Similarly, a derivative of the diphenyl phosphorazidate has been reported⁸ to produce only the reduction product upon triplet sensitization. Apparently, the energy transfer is more efficient in this case. Thus, assuming that both azides are mechanistically equivalent, the triplet azide and the triplet nitrene do not populate the corresponding singlet intermediates efficiently.

According to this analysis, the rate of the intersystem crossing (k_{1C}) of the singlet nitrene can be evaluated from the slope (equal $(r + 1)k_{1C}/k_i$) of the plot in Figure 1b. Within experimental error, hydrocarbon **2** undergoes insertion with the total rate constant (k_i), which is diffusion-limited.²⁹ Substituting $k_i \approx k_{diff}$, an estimate of the rate constant for intersystem crossing may be obtained. At 8×10^8 s⁻¹—or taking into account that a collision with a solvent molecule is necessary, at 2×10^8 M⁻¹ s⁻¹ in 4.94 M perfluorohexane—this rate is remarkably slow (see below).

Singlet Nitrene Selectivity. Solvation. It is noteworthy that the insertion selectivity (k_3/k_1) of the nitrene in perfluorohexane is almost double that observed in the hydrocarbon solvent. This increase in selectivity is attributed to a specific solvation of the singlet state of **1**. The electron-deficient p orbital of the singlet interacts with nonbonding electrons of a fluorine atom, forming a complex. For reactions with early transition states (see above), the increased selectivity must be mostly due to the solvation of the reactant(s) and not the transition state. It is not at all surprising that an electron-deficient nitrene will be affected by the solvent with unshared electrons. Similar phenomena were observed for other nitrenes³⁰ and analogous solvation has been proposed for methylene.¹³ These observations suggest that it might be impossible to observe an uncomplexed intermediate of this kind in an inert solvent.

Additionally, the interaction with the solvent has important consequences for multiplicity of the reacting intermediate. The nitrene-solvent complexation is expected to stabilize the singlet state, thus diminishing the thermodynamic driving force for intersystem crossing to the triplet state.³¹ It also reduces spin-orbit

(26) A similar trend would be observed for triplet azide-triplet nitrene, an unlikely alternative.

(27) A reversible intersystem crossing would provide a linear correlation with a nonzero intercept (Appendix B).

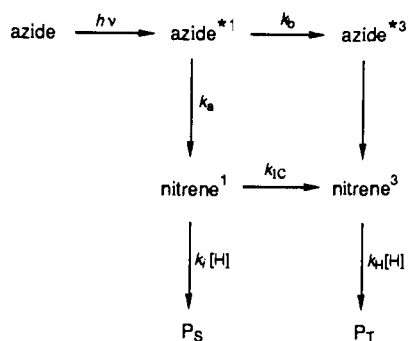
(28) It is expected (see ref 13) that the triplet azide would be efficiently quenched by oxygen (energy transfer) resulting in diminished rate of azide consumption in experiments run under oxygen. Since the efficiency of reaction under O₂ is only very slightly reduced as compared to that under argon, the triplet azide must lose nitrogen rapidly leading to the triplet nitrene.

(29) The estimated total rate of insertion of **1** into **2** is $0.97k_{diff}$. For such ferocious intermediates, it is often simply assumed that $k_{obs} = k_d$.

(30) For a review see: Lwowski, W. In *Reactive Intermediates*; Jones, M., Jr., Moss, R. A., Ed.; Wiley: New York, 1980; Vol. 2, p 315.

(31) Nitrenes are believed to have triplet ground states. All nitrenes studied so far (with exception of aminonitrenes) confirm that generalization. See ref 19 for a review.

Scheme II



coupling in the complexed nitrene,¹¹ lowering the probability of the spin-flip. This diminished driving force and the inefficient mechanisms for change of spin states are reflected in the rather slow rate of the intersystem crossing (see above).

Summary and Conclusions

The proposed test for diffusion-limited reactions provides a new tool to explore solution dynamics of reactive intermediates. This test evaluates the probability of reaction within the encounter complex, providing a new method to explore cage efforts in reactions not involving radical coupling. In practice, the test may be limited by the requirement for two substrates with identical diffusive properties but containing an unequal number of reactive sites. For many reactions, such substrates will have to be synthesized. Fortunately, diffusion coefficients of typical organic molecules with similar sizes do not differ significantly. Nevertheless, special care in the selection of substrates has to be exercised, especially in systems where the reactive groups may interact with solvent, for example, via hydrogen bonding. Also, the test in its simple form is not well suited for reversible reactions, such a proton- or electron-transfer processes. Finally, some mechanistic information about the tested process is required. The test may not be applicable to very complex mechanisms with many kinetically significant steps.

It has been demonstrated here, however, that the method can be applied to a quite complex experimental system involving two interconverting reactive intermediates reacting with substrates with multiple sites. To improve the precision of the test, substrates may be developed that will involve only one kind of reacting site. The test can be also easily extended to different kinds of reactions of interest³² and may find application in kinetics in heterogeneous media where direct measurements are difficult or impossible.

The utility of the test has been demonstrated on an example of photogenerated ferocious intermediate, (diethoxyphosphoryl)nitrene, **1**. Together with accompanying mechanistic studies, this test produced a detailed mechanistic picture of reactivity of this nitrene in the inert solvent (Scheme II). Direct irradiation of the azide leads to efficient production of the singlet azide. Apparently, this intermediate loses nitrogen in competition with the intersystem crossing to the triplet azide. The relative rates of these competing processes are ca. 3:1. Both singlet and triplet azides lose nitrogen rapidly and are intercepted by oxygen only very inefficiently. The singlet nitrene is specifically solvated by perfluorohexane. This solvation accounts for the rather low rate of its intersystem crossing to the triplet nitrene ($k_{IC} = 8 \times 10^8 \text{ s}^{-1}$) and its increased selectivity as compared to that observed in hydrocarbon solvent. The oxygen-insensitive, complexed, singlet nitrene inserts stereoselectivity into tertiary C-H bonds with an estimated rate of $0.3k_d = 3 \times 10^9 \text{ s}^{-1} \text{ M}^{-1}$ per bond. Thus, the insertion reaction of the singlet nitrene successfully competes with the intersystem crossing to the triplet nitrene. The triplet nitrene produced via this pathway, or from the triplet azide, abstracts hydrogen but does not contribute to the insertion reaction. The triplet nitrene itself, or a radical derived from it via hydrogen abstraction, is efficiently trapped by oxygen.

Experimental Section

¹H NMR spectra were recorded in CDCl₃ on a Bruker WP-200 (200-MHz) or Bruker AM-300 (300-MHz) spectrometer as specified. Spectra are reported in ppm referenced to TMS. Infrared (IR) spectra were obtained with a Perkin-Elmer Model 281B infrared spectrometer and are reported in inverse centimeters. Mass spectral analyses (MS) were recorded with a Kratos MS 9/50 double-focusing spectrometer in the electron impact (EI) or chemical ionization (CI) mode. Argon passed through an oxygen-removal catalyst (BASF) was used to deoxygenate the solvents and was used in inert atmosphere experiments.

Analytical gas chromatography was carried out on a FID-equipped Hewlett-Packard Model 5890 gas chromatograph using a 30-m DB-5 capillary column (J & W Scientific) in an isothermal mode (150 °C for reactions with **2** and **3**, 180 °C for reactions with dimethylcyclohexane). The column head pressure was 13 psi, and helium was used as a carrier gas. Preparative gas chromatography was performed at 150 °C with a Model 920 Varian aerograph and a 10% OV-17 on 80/100 Supelcoport 6-ft \times 1/4-in. column. The chromatographs were vented to a laboratory hood (*toxic materials involved!*).

Diethyl phosphorazidate was prepared according to the literature procedure.¹⁰ *Caution! The azide is highly toxic.*^{7,10} Hydrocarbons **2**, **3**, *cis*-**10**, *trans*-**10**, cyclohexane, and cyclohexane-*d*₁₂ were obtained from Aldrich. The selectively deuterated cyclohexane-*1,1,2,2,3,3,3-d*₆ was obtained from Merck Sharp & Dohme Isotopes (Canada). The perfluorohexane samples were obtained from Aldrich, PCR, and Columbia Organic Chemicals. All the reactions in perfluorohexane were run below the solubility limit of the hydrocarbons. Observations that the selectivity of insertion was different in the hydrocarbon solvent and in perfluorohexane and that the selectivity was independent of hydrocarbon concentration assure that reactions were homogeneous.

Nitrene **1** was produced by photolysis of the corresponding azide at 22 °C (see below). The products of the reaction with hydrocarbons were separated by preparative GC and identified by NMR and MS. All *N*-alkylamides showed very similar IR spectra: 3110 (m), 2940 (s), 1460 (s), 1240 (s), 1055 (s), 955 (s), 785 (m).

The reaction of **1** with **2** gave three products (retention times, minutes): **9** (4.3), **4** (9.8), and **5** (13.3). These were separated and identified by comparison with authentic samples (in case of **9**) or by spectral analysis.

Amide 4. NMR (200 MHz): 4.07, m, 4 H; 2.32, br s, 1 H; 1.69, septet, $J = 6.8 \text{ Hz}$, 1 H; 1.32, t, $J = 7.1 \text{ Hz}$, 6 H; 1.19, s, 6 H; 0.90, d, $J = 6.8 \text{ Hz}$, 6 H. MS-EI (m/e , relative intensity): 237 (P^+ , 0.4), 222 (6), 194 (100), 166 (16), 138 (36), 120 (7), 98 (8). MS-CI: 236 ($P-1$, 1), 222 (6), 194 (100), 166 (21), 138 (45), 120 (8). Precise molecular weight calculated for [C₁₀H₂₄NO₃P]-H: 236.1415. Found: 236.1426.

Amide 5. NMR (200 MHz): 4.06, m, 4 H; 2.89–2.66, m, 2 H; 2.29, s, 1 H; 1.65, m, 1 H; 1.42, m, 1 H; 1.33, t, $J = 7.1 \text{ Hz}$, 6 H; 0.90, d, $J = 6.8 \text{ Hz}$, 3 H; 0.85, d, $J = 6.8 \text{ Hz}$, 3 H; 0.82, d, $J = 6.7 \text{ Hz}$, 3 H. MS-EI: 237 (P^+ , 3), 222 (1), 194 (4), 166 (100), 154 (11), 138 (20), 122 (9), 110 (29). MS-CI: 237 (P^+ , 2), 194 (2), 166 (100), 154 (10), 138 (24), 122 (10), 94 (7). Precise molecular weight calculated for C₁₀H₂₄NO₃P: 237.1494. Found: 237.1495.

The reaction of **1** with **3** gave four products (retention times, minutes): **9** (4.3), **6** (12.6), **7** (16.9), and **8** (17.1). The last two could not be completely separated by the preparative GC. They also gave partially overlapping peaks on the capillary column.

Amide 6. Mp 58–60 °C. NMR (200 MHz): 4.11, dq, $J = 7.0 \text{ Hz}$, $J = 7.9 \text{ Hz}$, 4 H; 2.25, br s, 1 H; 1.32, t, $J = 7.0 \text{ Hz}$, 6 H; 1.24, s, 6 H; 0.94, s, 9 H. MS-EI: 236 (7), 206 (2), 194 (100), 166 (14), 138 (36), 120 (6), 98 (7). MS-CI: 250 ($P-1$, 0.3), 236 (7), 206 (2), 194 (100), 166 (17), 138 (32), 120 (6), 98 (5). Precise molecular weight calculated for [C₁₁H₂₆NO₃P]-H: 250.1572. Found: 250.1567.

Amide 7. NMR (300 MHz): 4.07, m, 4 H; 3.08, ddd, $J = 12.5 \text{ Hz}$, $J = 7.1 \text{ Hz}$, $J = 3.2 \text{ Hz}$, 1 H; 2.48, ddd, $J = 12.5 \text{ Hz}$, $J = 10.2 \text{ Hz}$, $J = 10.1 \text{ Hz}$, 1 H; 1.93, br s, 1 H; 1.90, m, 1 H; 1.33, t, $J = 7.0 \text{ Hz}$, 4 H; 0.92, d, $J = 6.8 \text{ Hz}$, 3 H; 0.88, s, 9 H.

Amide 8. NMR (300 MHz): 4.07, m, 4 H; 2.72, d, $J = 6.6 \text{ Hz}$, 2 H; 1.93, br s, 1 H; 1.56, septet, $J = 6.8 \text{ Hz}$, 1 H; 1.33, t, $J = 7.8 \text{ Hz}$, 4 H; 0.84, d, $J = 6.8 \text{ Hz}$, 6 H; 0.82, s, 6 H. MS-EI (mixture of **7** and **8**): 251 (P^+ , 3), 236 (1), 208 (3), 194 (3.5), 166 (100), 154 (4), 138 (17), 122 (7), 110 (21) 98 (4), 94 (4) 86 (5). MS-CI: 251 (P^+ , 1), 208 (3), 194 (3), 166 (100), 154 (2), 152 (3), 138 (20), 126 (2), 122 (8), 98 (4), 94 (6). Precise molecular weight calculated for C₁₁H₂₆NO₃P: 251.1650. Found: 251.1651.

The reaction of **1** with cyclohexane gave **9** and diethyl *N*-cyclohexylphosphoramidate (retention time: 19.5 min at 150 °C). The authentic sample of this material was prepared as described previously.⁷

The reaction of **1** with *cis*-**10** produced a mixture of products that—in addition to **9**—included (retention times in minutes at 180 °C) a single tertiary C-H-derived amide (12.2), four overlapping secondary C-H-

derived amides (13.4, 13.8, 14.2, 14.5), and a single primary C-H-derived amide (17.0). Similarly, *trans*-10 gave one tertiary C-H-derived amide (11.0), four secondary C-H-derived amides (12.6, 12.8, 12.9, 13.3), and a single primary C-H-derived amide (15.2). Assuming identical detector response factors for all these compounds, the calculated selectivities (tertiary:secondary:primary) are 1:0.6:0.19 or 1:0.4:0.1 for *cis* and 1:0.6:0.18 or 1:0.4:0.1 for *trans*, in hydrocarbon or fluorinated solvents, respectively. The tertiary C-H-derived amides were found to be identical with the two amides resulting from the reaction between diethoxyphosphoryl chloride and the mixture of *cis*- and *trans*-1,2-dimethylcyclohexylamines.¹⁵ The primary and secondary C-H-derived amides were not analyzed. The tertiary C-H-derived amides were easily separated by the GC. No amide (<1%) with a retention time of 11.0 was detected for the *cis* compound, and no amide with a retention time of 12.2 was observed in the reaction of the *trans* compound, either in hydrocarbon solution or in perfluorohexane, indicating that the reaction is completely stereospecific. Similar *trans* products usually have shorter retention times,¹⁴ and therefore, retention of the configuration is the implicated course of the insertion reaction. A study to strictly elucidate absolute stereochemistry of the insertion is in progress and will be reported elsewhere.

For reactions under an argon atmosphere, all reagents and solvents were deoxygenated prior to mixing, and for reactions run under O₂, they were saturated with oxygen. The reaction samples were prepared in argon-filled (or oxygen-filled) 3-mL quartz test tubes closed with sub-seal septa (Aldrich). The solvents and reagents were transferred via gas-tight syringes. For competition experiments, a measured volume of a solution of the azide in perfluorohexane was transferred to the sealed test tube. Then, appropriate volumes of hydrocarbons were injected. The total volume of the sample was ca. 3.0 mL to minimize the empty space

above the solution. The samples were irradiated for 25–50 min at 22 °C on a merry-go-round with a 450-W medium-pressure Hanovia lamp through a Vycor filter. The solution of internal standard (tetradecane) was then injected, and the volatiles (solvent) were removed at 20 °C under reduced pressure. The residue was dissolved in CH₂Cl₂ and analyzed by GC. The yields of all reactions were determined after corrections for detector response. The calibration was performed with the authentic samples of reaction products by multiple injection. The concentration of the azide stock solution was determined in the same way. The results obtained for the azide (retention time 3.9 min) were in excellent agreement with those calculated from the weight of the azide used to prepare the stock solution. Double injection was used to determine the products yields for most samples. The data for runs 21, 22, 25, and 27 in Table II were obtained from six or seven injections. The reproducibility of the data was good. Average values are listed in Tables I–III.

A similar procedure was followed for reactions run in a hydrocarbon solvent. The isotope effects were obtained by multiple analysis of samples by mass spectrometry. The starting mixtures of cyclohexane-*h*₁₂/cyclohexane-*d*₁₂ as well as cyclohexane-*d*₆ were analyzed on the same instrument. The amide hydrogens were completely exchanged prior to the analysis.

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Supplementary Material Available: Appendices A and B containing derivation of the kinetic equations used (5 pages). Ordering information is given on any current masthead page.

Photochemical Transformations. 48. The Nonconcertedness of Nucleofuge Loss and *anti*-Aryl Migration in Photochemical Wagner–Meerwein Rearrangements¹

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Abstract: Preparation of the two diastereomers of 3-(3,5-dimethoxyphenyl)-2-butanol and of their 2-deuterio analogues has been carried out. When the methanesulfonate esters of the diastereomers were solvolyzed by heating at reflux in 50% aqueous methanol, the resulting alcohols and methyl ethers were formed with complete retention of diastereomeric identity and without measurable hydride migration to give the 2-aryl-2-butyl isomer. Similar treatment of the methanesulfonates of the deuterio analogues gave complete deuterium scrambling, that is, gave equal mixtures of 3-aryl-2-deuterio-2-butyl and 3-aryl-3-deuterio-2-butyl derivatives. These results of ground-state solvolyses are consistent with aryl participation coincident with nucleofuge loss, with bridged phenonium ions as sole intermediates. On the other hand, irradiations of the methanesulfonates with 300-nm light in the same solvent gave photosolvolysis with considerable diastereomeric mixing, although again complete deuterium scrambling was observed here as well. In addition, significant amounts of 2-aryl-2-butanol were formed. The excited-state results require a much more complicated reaction course than the ground-state results, probably involving *syn*-hydrogen migration to give the tertiary alcohol, along one path, and requiring that the observed aryl migrations, along another path, occur later than, rather than concerted with, nucleofuge loss.

Since the first example of photosolvolysis involving carbocations of β -arylethyl (homobenzyl) systems was reported by Jaeger,² members of our research group,³ as well as others,^{4,5} have devoted

considerable effort in elucidating the mechanism of these intramolecular excitation-transfer processes, which result in the activation of remote functional groups. Although the first example reported by Jaeger² dealt with an acyclic homobenzyl system, almost all of the work done in the intervening years involved cyclic systems.^{3–5} Much has been learned from these studies and from

(1) Part 47: Cristol, S. J.; Vanden Plas, B. J. *J. Org. Chem.* **1989**, *54*, 1209.

(2) Jaeger, D. A. *J. Am. Chem. Soc.* **1976**, *98*, 6461.

(3) (a) Cristol, S. J.; Stull, D. P.; Daussin, R. D. *J. Am. Chem. Soc.* **1978**, *100*, 6674. (b) Cristol, S. J.; Opitz, R. J.; Bindel, T. H.; Dickenson, W. A. *Ibid.* **1980**, *102*, 7977. (c) Cristol, S. J.; Dickenson, W. A.; Stanko, M. K. *Ibid.* **1983**, *105*, 1218. (d) Cristol, S. J.; Seapy, D. G.; Aeling, E. O. *Ibid.* **1983**, *105*, 7337. (e) Cristol, S. J.; Ali, M. Z. *Tetrahedron Lett.* **1983**, 5839. (f) Cristol, S. J.; Aeling, E. O.; Heng, R. *J. Am. Chem. Soc.* **1987**, *109*, 830 and references therein.

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(5) Jaeger, D. A.; Bernhardt, E. A. *Tetrahedron Lett.* **1983**, *24*, 4521.