Table I. Bimolecular Rate Constants, Efficiencies, Energies,[a] and α's for $ArCH_2^- + CH_3Br$

substituent	ΔE_{rxn}[b]	k_{bim}[c]	efficiency, %	ΔE_o^*	ΔE_o^*	α
p-Me	−60.4	39.7	32.8	2.25	22.2	0.16
H	−58.9	23.1	18.5	2.85	22.8	0.18
m-F	−53.5	7.65	6.4	3.75	22.6	0.20
m-CN	−48.0	1.10	0.9	5.10	22.8	0.24

[a] As defined in Figure 1; units of kcal/mol. [b] Reference 12. [c] Units of 10^{-11} cm^3 molecule^{-1} s^{-1}.

constants k_{bim} obtained by monitoring benzyl anion depletion and bromide ion appearance were similar. The rate constants and efficiencies (efficiency = k_{bim}/k_{coll}, where k_{coll} is the ion–neutral collision rate constant[11]) are listed in Table I, along with overall energies of reaction[12,14] ΔE_{rxn}.

Experimental evidence[3] indicates that low-efficiency gas-phase nucleophilic processes occur along reaction coordinates with double minima. The rate of a reaction following such a potential surface is less than unit efficient due to the existence of the barrier between the wells. This situation has been shown to be amenable to an RRKM analysis.[3] By using frequencies and moments of inertia for the orbiting and S_N2 transition states as input parameters, and by matching experimental values of the branching fractions, one obtains the energy of the S_N2 transition state relative to that of the separated reactants[3] (Figure 1). Estimation of the $ArCH_2^-/CH_3Br$ well depths[15,16] as a constant 7.5 kcal/mol allows a determination of the activation energies ΔE^*. A plot of ΔE^* vs. ΔE_{rxn} (obtained by independent measurements[13]) gives a slope of 0.2. The slope is insensitive to the RRKM input parameters and independent of the well depth, provided the well depth is constant.

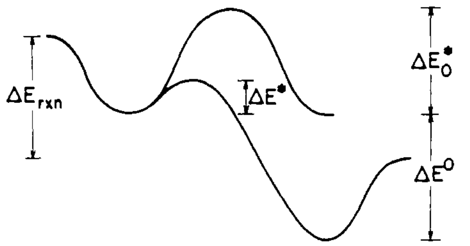

Figure 1. Relationship among the quantities ΔE^*, ΔE_o^*, and ΔE° in the Marcus equation, in the context of an exothermic gas-phase S_N2 reaction with a double-minimum potential.

For the application of the Marcus equation, ΔE° for the "intrinsic" methyl transfer step must be estimated.[17] Since the overall exothermicity is so large, however, the expected small[18] variation in the $Br^-/ArCH_2CH_3$ well depths does little to affect the calculated value of the intrinsic barrier ΔE_o^*. More important are the choices for the RRKM input parameters. The parameters for the orbiting complex are well-defined;[19] therefore most of the uncertainty lies in the structure and vibrational frquencies of the S_N2 transition state, which give rise to different values of ΔE^*. Nonetheless, the values of ΔE^* are fairly insensitive to S_N2 transition-state entropy. Thus, the values of α are also insensitive to changes in S_N2 transition-state entropy, since they are calculated from the values of ΔE^* through eq 1. Varying the entropy as much as 25 eu (an enormous range for RRKM calculations[20]), by altering the frequencies of the three vibrations most sensitive to changes in structure and bonding, results in α varying only from 0.22 to 0.18. The values of ΔE^*, ΔE_o^*, and α are listed in Table I, taking $\Delta E^\circ = \Delta E_{rxn}$ and using S_N2 transition-state parameters about midway through the entropy range investigated. The plot of ΔE^* vs. ΔE° is linear, with a slope of ~0.2 as predicted from the Marcus intrinsic activation energy ΔE_o^* and the overall exothermicity, ΔE°.

In conclusion, we have demonstrated the consistency of the Marcus equation in application to S_N2 reactions by showing that the value of α predicted by the Marcus equation correctly predicts the slope of a Brønsted plot.[21] Our results thus strongly support the idea that the activation energy can indeed be considered as the sum of an intrinsic activation energy plus a term associated with the overall exothermicity of the reaction. Accordingly, our calculation[3] of these intrinsic barriers appears justified.

Acknowledgment. We are grateful to the National Science Foundation for support of this research and for fellowship support to J.A.D. We thank Professor R. W. Taft (U.C., Irvine) for informing us of his results on toluene acidities, and Professor P. Kebarle (Alberta) for helpful discussions.

Registry No. F^-, 16984-48-8; $ArCH_2^-$ (Ar = *p*-MeC_6H_4), 59305-42-9; $ArCH_2^-$ (Ar = Ph), 18860-15-6; $ArCH_2^-$ (Ar = *m*-FC_6H_4), 72611-56-4; $ArCH_2^-$ (Ar = *m*-NCC_6H_4), 72611-58-6; CH_3Br, 74-83-9; *m*-cyanotoluene, 620-22-4; *p*-methylbenzyltrimethylsilane, 7450-04-6; benzyltrimethylsilane, 770-09-2; *m*-fluorobenzyltrimethylsilane, 772-48-5.

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(10) Benzyl anions were generated by reaction of F^- with an appropriate precursor, either the toluene (*m*-CN) or benzyltrimethylsilane (*p*-Me, H, *m*-F). Corrections were made for ion loss and for reaction of F^- with CH_3Br.

(11) (a) Su, T.; Bowers, M. T. *Int. J. Mass Spectrom. Ion Phys.* **1973**, *12*, 347–356. (b) Su, T.; Bowers, M. T. In "Gas Phase Ion Chemistry"; Bowers, M. T.; Ed.; Academic Press: New York, 1976; Vol. 1.

(12) ΔE_{rxn} for the unsubstituted benzyl anion was determined from Benson's values (Benson, S. W. "Thermochemical Kinetics", 2nd ed.; Wiley-Interscience: New York, 1976) and the known electron affinity of benzyl radical (Richardson, J. H.; Stephenson, L. M.; Brauman, J. I. *J. Chem. Phys.* **1975**, *63*, 74–76. Drzaic, P. S.; Brauman, J. I. *J. Phys. Chem.*, in press). For the substituted anions E_{rxn} was calculated from the known acidities of toluenes[13] and the assumption of constant C_α–H and C_α–C_β bond strengths in toluenes and ethyl benzenes, respectively.

(13) Taft, R. W., Mashima, M., personal communication.

(14) We assume that alkylation is occurring at the α-carbon. See: Russell, G. A. *J. Am. Chem. Soc.* **1959**, *81*, 2017–2022.

(15) (a) Dougherty, R. C.; Roberts, J. D. *Org. Mass Spectrom.* **1974**, *8*, 81–83. (b) Kebarle, P., personal communication.

(16) In the absence of strong hydrogen bonding the ion–neutral well depths are relatively independent of ion structure.[18]

(17) Potential energies have been substituted for free energies.[2,3b]

(18) French, M. A.; Ikuta, S.; Kebarle, P. *Can. J. Chem.* **1982**, *60*, 1907–1918.

(19) Olmstead, W. N.; Brauman, J. I. *J. Am. Chem. Soc.* **1977**, *99*, 4219–4228.

(20) (a) Forst, W. "Theory of Unimolecular Reactions"; Academic Press: New York, 1973. (b) Robinson, P. J.; Holbrook, K. A. "Unimolecular Reactions"; Wiley-Interscience: New York, 1972.

(21) Two reports suggesting legitimacy of the application of the Marcus equation to solution-phase group transfer reactions have appeared since submission of our manuscript: Kreevoy, M. M.; Lee, I.-S. H. *J. Am. Chem. Soc.* **1984**, *106*, 2550–2553. Lewis, E. S.; Hu, D. D. *J. Am. Chem. Soc.* **1984**, *106*, 3292–3296.

Useful Chiral Packing Materials for High-Performance Liquid Chromatographic Resolution of Enantiomers: Phenylcarbamates of Polysaccharides Coated on Silica Gel[1]

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Resolution of enantiomers by liquid chromatography on chiral stationary phases has become a practically useful method for obtaining optical isomers and determining their purities.[2] Microcrystalline cellulose triacetate, which is prepared by heterogeneous acetylation,[3] is a useful stationary phase and has been widely employed for the resolution of aromatic compounds.[4]

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(1) Chromatographic Resolution 7. Part 6: ref 5.

(2) (a) Blaschke, G. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 13. (b) Pirkle, W.; Finn, J. "Asymmetric Synthesis"; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 1, p 87.

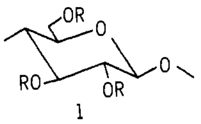
(3) (a) Hesse, G.; Hagel, R. *Chromatographia*, **1973**, *6*, 277. (b) Hesse, G.; Hagel, R. *Liebigs Ann. Chem.* **1976**, 996.

Table I. Chromatographic Resolution of **8–10** and DPO on Phenylcarbamates (**1–7**) of Polysaccharides[a]

	8			**9**			**10**			DPO[b]		
column	k_1'	α	Rs	k_1'	α	Rs	k_1'	α	Rs	k_1'	α	Rs
1	1.42 (−)	1.47	1.38	1.02(+)	1.39	1.73	2.24 (+)	1.31	0.75	0.85 (+)	1.53	2.00
2	0.61	1.00		0.77 (+)	1.28	1.10	1.80 (−)	1.28	0.87	0.39 (+)	1.46	1.29
3	0.55 (−)	2.25	2.97	1.19	1.00		4.90 (+)	≈1		0.68 (+)	1.37	1.39
4	1.25 (−)	2.69	2.67	0.67 (−)	1.26	1.00	3.27 (−)	1.17	0.72	0.32 (+)	1.45	1.17
5	0.61 (+)	≈1		0.67 (+)	1.23		2.30 (+)	≈1		0.23 (+)	1.41	1.15
6	0.59	1.00		0.67 (+)	1.13	0.49	3.39 (−)	2.32	2.64	0.29	1.00	
7	0.66	1.00		0.71 (−)	≈1		3.32 (+)	1.51	1.96	0.29	1.00	

[a] Conditions are shown in Figure 1; k_1' (capacity factor for less retained enantiomer) = (retention time - dead time)/dead time, α (separation factor) = (capacity factor for more retained enantiomer)/k_1', Rs (resolution factor) = 2 × (distance of the two peak positions)/(sum of bandwidths of the two peaks). [b] *trans*-2,3-Diphenyloxirane.

Hesse and Hagel stated that its chiral recognition capability was substantially reduced once the triacetate was dissolved in a solvent.[3] However, we found that cellulose triacetate adsorbed on silica gel from solution showed a chiral recognition capability completely different from that of microcrystalline cellulose triacetate;[5] enantiomers of Tröger base were eluted in reversed order on the two triacetate columns. In this communication, we wish to report chiral packing materials for high-performance liquid chromatography (HPLC) prepared with phenylcarbamates of various polysaccharides: cellulose (**1**), amylose (**2**), chitosan (**3**), xylan (**4**), curdlan (**5**), dextran (**6**), and inulin (**7**). Some of the packing materials showed remarkable resolution ability and high durability.



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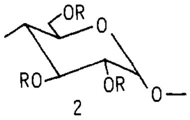

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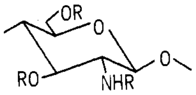

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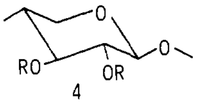

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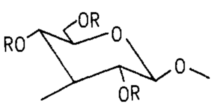

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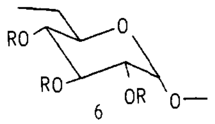

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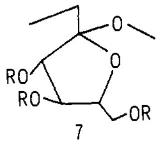

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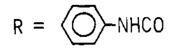

The phenylcarbamates **1–7** were prepared by the reaction of a large excess of phenyl isocyanate with the corresponding polysaccharides in pyridine at about 100 °C. Elemental analysis, ^{1}H NMR, and IR spectra indicate that almost all hydroxy groups of the polysaccharides were converted into urethane bonds. Macroporous silica gel (Merck, LiChrospher SI 4000, 10 μm) was treated with a large excess of (3-aminopropyl)triethoxysilane and coated with about 20 wt % of a phenylcarbamate in the same manner as described in the previous paper.[6] The packing materials thus obtained were packed in a stainless steel column (25 × 0.46 (i.d.) cm) by the slurry method.[7]

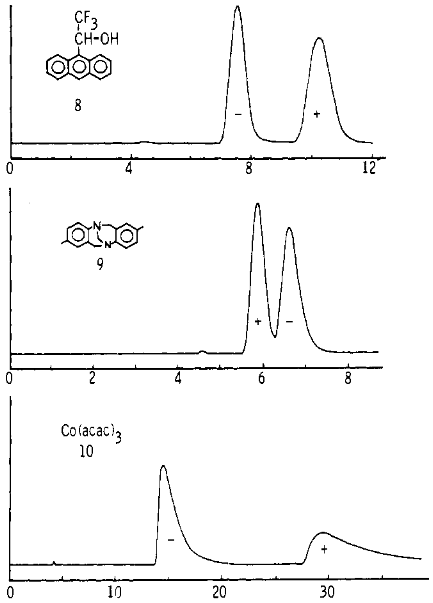

Figure 1. Chromatographic resolution of **8**, **9**, and **10** on the columns of **1**, **2**, and **6**, respectively. Columns 25 × 0.46 (i.d.) cm; eluant, hexane–2-propanol (90:10) (0.5 mL min^{-1}); temperature 25 °C.

Figure 1 shows the chromatograms of resolution of 1-(9-anthryl)-2,2,2-trifluoroethanol (**8**), Tröger base (**9**), and cobalt(III) tris(acetylacetonate) (Co(acac)$_3$, **10**) on columns of **1**, **2**, and **6**, respectively; the results of resoltuion of these compounds and *trans*-2,3-diphenyloxirane (DPO) on the phenylcarbamate columns are summarized in Table I. The chiral discrimination of the stationary phases was highly dependent on the polysaccharides; **1** and **4** resolved all the racemic compounds in Table I, while **7** resolved only **10** with a high efficiency. It is noted that **4** and **6** showed remarkable chiral discrimination against **8** and **10**, respectively. The resolution of **8** has been achieved on the chiral stationary phases derived from phenylglycine[8] and (+)-poly(triphenylmethyl methacrylate),[6] which showed α = 1.33 and 1.67, respectively. Complex **10** has been resolved on several chiral stationary phases.[9] The separation described here seems to be the most effective one. The cellulose triacetate coated on silica gel could separate **9** and DPO, but not **8** and **10**.[5]

Besides the compounds listed in Table I, the column of **1** resolved many of the racemic compounds that were separable on (+)-poly(triphenylmethyl methacrylate).[6] This column also exhibited resolving power for **9** (k_1' = 1.30 (+), α = 1.21, Rs = 0.9)

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(4) (a) Häkli, H.; Mintas, M.; Mannschreck, A. *Chem. Ber.* **1979**, *112*, 2028. (b) Schlögl, K.; Widhalm, W. *Ibid.* **1982**, *115*, 3042. (c) Koller, H.; Rimböck, K.-H.; Mannschreck, A. *J. Chromatogr.* **1983**, *282*, 89 and references cited therein.

(5) Okamoto, Y.; Kawashima, M.; Hatada, K. *Chem. Lett.* **1984**, 739. A similar result has also been obtained by the researchers of Daicel Chemical Industries Ltd.: Shibata, T.; Nakamura, H.; Okamoto, I.; Namikoshi, H. 49th National Meeting of the Chemical Society of Japan, Tokyo, April 1984, Abstr. No. 2M42.

(6) Okamoto, Y.; Honda, S.; Okamoto, I.; Yuki, H.; Murata, S.; Noyori, R.; Takaya, H. *J. Am. Chem. Soc.* **1981**, *103*, 6971.

(7) The columns had 4000–7000 theoretical plates for a weakly retained compound. The chromatography was accomplished on a JASCO TRIROTAR II chromatograph equipped with a UV detector and a JASCO DIP-181C polarimeter detector (365 nm, cell 5 cm × 0.30 (i.d.) cm).

(8) Pirkle, W. H.; Finn, J. M. *J. Org. Chem.* **1981**, *46*, 2935.

(9) Okamoto, Y.; Honda, S.; Yashima, E.; Yuki, H. *Chem. Lett.* **1983**, 1221 and references therein.

and DPO (k_1' = 1.85 (+), α = 1.31, Rs = 1.58) using a mixture of ethanol-water (70:30) as eluant.[10] However, in most cases, hexane-2-propanol mixtures were better eluants than ethanol-water mixtures, suggesting that the hydrogen bond and/or dipole-dipole interaction between the stationary phase and racemic compounds play an important role for chiral discrimination. All the packing materials were quite stable under the experimental conditions shown in Figure 1.[11] Phenylcarbamate[12] of β-cyclodextrin was also adsorbed on silica gel and employed as a chiral stationary phase using hexane-2-propanol (99:1) as eluant. No separation was observed with a UV detector, although partial separation was found with a polarimeter detector. This suggests that higher order structures of polysaccharides may be important for effective chiral discrimination.

The present results in addition to the previous one[5] indicate that the various derivatives of polysaccharides will provide useful chiral packing materials especially when they are coated on silica gel.

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(10) The column was stable for at least 2 days in this eluant.

(11) The columns were not damaged by water present in hexane-2-propanol mixtures. The phenylcarbamates of low molecular weight may be soluble in ethanol-water mixtures.

(12) This was prepared in the same manner as in the cases of polysaccharides. Elemental analysis indicated that all hydroxy groups were converted into phenylcarbmate groups.

Loss of the Normal Intramolecular Preferential Reactivity with a Highly Nonselective Nitrene

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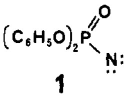
One of the striking successes of transition-state theory has been its explanation of the very high effective concentrations often observed with neighboring groups.[1] Reaction with a group within the same molecule is normally much faster than reaction with a chemically similar solvent; although collision frequencies with solvent molecules will generally be at least comparable to those with the neighboring group, intramolecular reactions are favored by the higher $\Delta S°$ in the activated complex. However, such effects should disappear if a highly reactive species is captured on almost every collision. Then collision frequencies ought to dominate the selectivity, since intrinsic to the idea of $\Delta S°$ is the reversibility of the formation of an activated complex. We have found behavior that seems to correspond to this prediction.

Some years ago[2] we described the photolysis of phosphorazidates to generate phosphorylnitrenes and the reaction of these nitrenes with hydrocarbon solvents. With 2-methylbutane, (diphenoxyphosphoryl)nitrene (**1**) showed a 3.4/1.2/1 preference for tertiary/secondary/primary hydrogens, making it the least selective nitrene known. For instance, (*tert*-butoxycarbonyl)nitrene shows a 160/9/1 preference.[3] However, in contrast to examples in which less selective nitrenes gave intramolecular attack on alkane chains in competition with attack on solvent,[4] we found in subsequent unpublished work[5] that our phosphorylnitrenes attacked only solvent. For example, photolysis of ethyl octyl phosphorazidate (**2**) in cyclohexane affords the cyclohexane nitrene insertion product in 86% yield, and hydrogen abstraction in 14% yield, but *no* detectable product from attack on the octyl chain. Even in CH_2Cl_2 or other chlorinated solvents no intramolecular product was detected, and the steroid derivatives **3** and **4** similarly underwent no steroid attack on photolysis. To explore the effect further, we have examined the nitrene **6** derived from bis(*o*-isopropylphenoxy) phosphorazidate (**5**).[6]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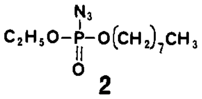
$C_2H_5O-\underset{\underset{O}{\|}}{\overset{\overset{N_3}{|}}{P}}-O(CH_2)_7CH_3$
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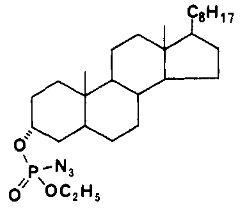
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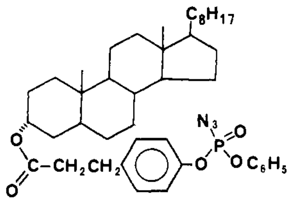
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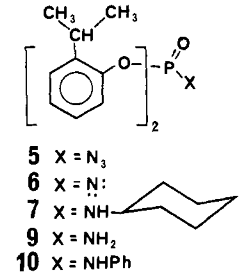

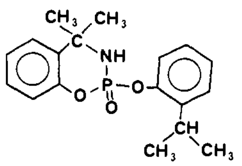
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The most striking observation was that direct photolysis of **5** (with a medium-pressure Hg lamp and Vycor filter) in cyclohexane solution afforded the cyclohexane insertion product **7**[6] in ca. 70% yield but no detectable amount of the cyclization product **8**[6] or of any other identifiable product resulting from intramolecular reactions. The product of nitrene reduction **9**[6] was also formed in ca. 12% yield. Assays were by G/C calibrated with authentically prepared samples of **7**–**9**; products were also confirmed by isolation and NMR comparison. Photolysis of **5** in CH_2Cl_2 or in tert-butyl alcohol produced various products from solvent attack but no detectable amount (less than 5%) of cyclization product **8**. Thus the nitrene **6** attacks solvent molecules preferentially instead of reacting with the neighboring isopropyl groups.[7]

When a less reactive version of **6** is generated, some intramolecular attack is seen. For instance, photolysis of **5** in benzene solution affords an easily detectable 3% of **8**, along with the major product **10**[6] from reaction with the solvent. This probably reflects stabilizing solvation of nitrene **6** by the benzene; similar results are seen in 1,3,5-trifluorobenzene solvent. Most strikingly, thermolysis of the azide **5** in benzene for 87 h at 120 °C with 15% by weight of dirhodium tetrapivalate[8] affords a 52 ± 8% yield of the cyclization product **8**. Apparently the rhodium-nitrene complex, a nitrenoid, is sufficiently unreactive to show the "normal" preference for intramolecular reactions predicted by transition-state theory.

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(1) Cf.: Page, M. I.; Jencks, W. P. *Proc. Nat. Acad. Sci. U.S.A.* **1971**, *68*, 1678.

(2) Breslow, R.; Feiring, A.; Herman, F. *J. Am. Chem. Soc.* **1974**, *96*, 5937.

(3) Cf.: Lwowski, W. "Nitrenes"; Wiley-Interscience: New York, **1979**; p 201.

(4) E.g.: Breslow, D. S.; Prosser, T. J.; Marcantoni, A. F.; Genge, C. A. *J. Am. Chem. Soc.* **1967**, *89*, 2384.

(5) For details, see: Herman, F. Ph.D. Thesis, Columbia University, 1975.

(6) All new compounds were synthesized by an unambiguous scheme and characterized by NMR and mass spectroscopy.

(7) It is hard to imagine a stereoelectronic preference that could explain the lack of intramolecular reaction for nitrenes derived from the entire set of compounds **2**–**5**. The distinction between singlet and triplet states for nitrenes can affect the relative yields of reduction vs. insertion products, but in our systems the striking finding is that the insertion reactions, characteristic of the singlet, prefer the solvent. This preference should in any case not be affected by multiplicity questions. When **5** was irradiated thru a Pyrex filter in cyclohexane with acetophenone as a triplet sensitizer, the principal product was **9**, from reduction of the nitrene, and neither **7** nor **8** could be detected.

(8) For the first report of a rhodium-catalyzed azide insertion reaction, see: Breslow, R.; Gellman, S. *J. Am. Chem. Soc.* **1983**, *105*, 6728.

0002-7863/84/1506-5359$01.50/0