β-glu, $K_I = 13.8 \pm 3\ \mu M$ at pH 5.6). Moreover the observed pH dependence of inhibition by **8** paralleled the variation in k_{cat}/K_M with pH for the enzyme (pH optimum = 5.6),[11] as expected for an ideal transition-state analogue inhibitior (Figure 1).

To our knowledge, amidoxime **8** is the first nonbasic saccharide analogue which mimics the true half-chair conformation of the glucosyl intermediate. The importance of the amidoxime's endocyclic double bond is evident when one compares **8** with D-gluconohydroximinolactone **4**,[4] whose functionality closely resembles **8** but whose exocyclic C=N bond creates a lactone-like conformation.[6] Compound **4** is a 7-fold weaker inhibitor of β-glu ($K_I = 98\ \mu M$).

Two important conclusions emerge from this work. First, it is apparent that the common structural elements of glucosyl mimics **6–8** (and their mannose analogues)[8] represent an "Achilles heel" in carbohydrate enzymology to which many simple glycosidases are vulnerable. Moreover levels of β-glu inhibition remain nearly constant despite a 10^5 change in basicity over the amidoxime–amidrazone–amidine series. Assuming that the exocyclic NH_2, $NHNH_2$, and NHOH groups of **6–8**, respectively, interact in similar ways with the β-glu active site (an assumption not devoid of risk),[12] we conclude that adopting the flattened anomeric conformation of the glucosyl intermediate is more important for transition-state binding by the enzyme than achieving the full-fledged charge of the glucopyranosyl cation. This observation should be useful in designing potent new inhibitors of glucoside hydrolysis.

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Supplementary Material Available: Experimental details (including physical properties, spectral and analytical data) for preparing **7** and **8** plus kinetic plots from enzymatic assays (6 pages). Ordering information is given on any current masthead page.

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(12) One referee has noted, for instance, that the absence of a positive charge on **8** might be compensated for by additional H-bonding to the enzyme. An X-ray crystal structure of the β-glu E–I complex should resolve these issues.

Interception of Dimethylcarbene with Pyridine: A Laser Flash Photolysis Study

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Dialkylcarbenes are notoriously difficult to intercept with external chemical trapping agents[1] and to detect by matrix isolation spectroscopy.[2] Presumably, this is due to their ability to undergo rapid intramolecular rearrangements. In fact these rearrangements have at times been considered to have zero enthalpic barrier. Indeed the question has been posed whether dialkylcarbenes are true reactive intermediates, or transition structures, or even nonstationary points on a potential surface connecting a carbene precursor with the product of rearrangement.[3]

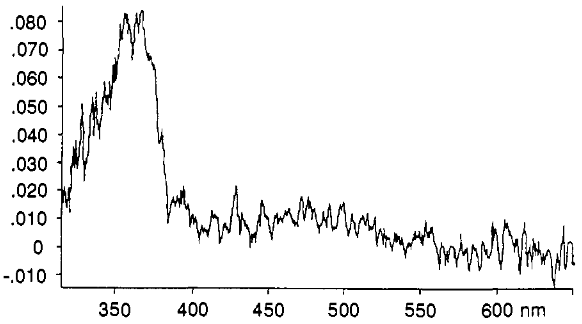
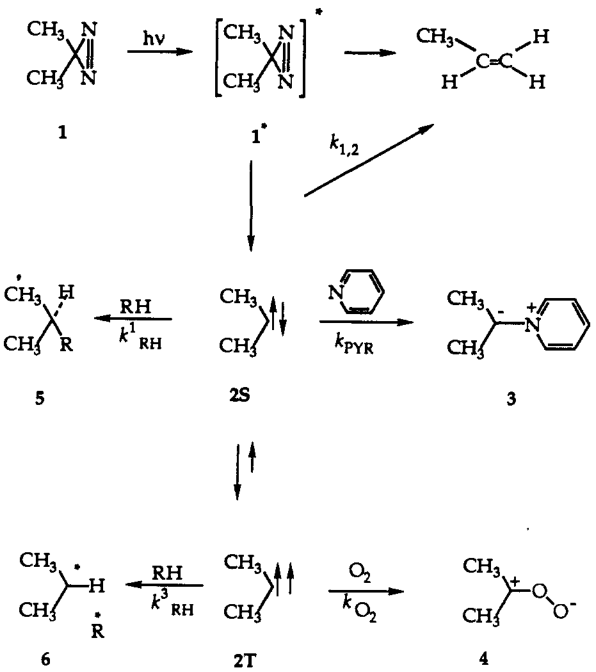


Figure 1. The transient spectrum of ylide **3** produced by LFP of 3,3-dimethyldiazirine (**1**) in *n*-pentane containing pyridine at 25 °C.

Scheme I



We have recently demonstrated that two dialkylcarbenes, adamantanylidene,[4] and homocubanylidene[5] can be intercepted with pyridine to form ylides which are easily detected by laser flash photolysis (LFP) techniques. These two carbenes can only rearrange to highly strained products which may account for carbene lifetimes that are sufficiently long to permit their capture with pyridine. However, Houk and Evanseck[6] have recently calculated that the activation barrier to isomerization of dimethylcarbene is 6.4 kcal/mol, which has prompted this study of this carbene by the pyridine probe method.

Laser flash photolysis (LFP)[7] of diazirine **1** (Lumonics excimer laser, XeF, 351 nm, 50 mJ) in *n*-pentane does not produce any detectable transient absorbance. However, LFP of **1** in the presence of pyridine produces the transient of Figure 1 which is

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(1) (a) Kirmse, W. K. *Carbene Chemistry*; Academic Press: New York, 1971. (b) *Carbenes*; Baron, W. J., DeCamp, M. R., Hendrick, M. E., Levin, R. H., Sohn, M. B., Moss, R. A., Jones, M., Jr., Eds.; Wiley: New York, NY, 1973; Vol. 1, p 1.

(2) See, for example: (a) Trozzolo, A. M.; Wasserman, E. *Carbenes*; Moss, R. A., Jones, M., Jr., Eds.; Wiley: New York, NY, 1975; Vol. 2, p 185. (b) Sheridan, R. S. *Organic Photochemistry*; Dekker: New York, NY, 1987; Vol. 8, p 159.

(3) (a) Schaefer, H. F. *Acc. Chem. Res.* **1980**, *73*, 3255. (b) Harding, L. B.; Schlegel, H. B.; Krishnan, R.; Pople, J. A. *J. Phys. Chem.* **1980**, *84*, 3394. (c) Pople, J. A.; Raghauechari, K.; Frisch, M. J.; Binkley, J. S.; Schleyer, P. V. R. *J. Am. Chem. Soc.* **1983**, *103*, 6389.

(4) Morgan, S.; Jackson, J. E.; Platz, M. S. *J. Am. Chem. Soc.* **1991**, *113*, 2782.

(5) Chen, N.; Jones, M., Jr.; White, W. R.; Platz, M. S. *J. Am. Chem. Soc.* **1991**, *113*, 4981.

(6) Evanseck, J. D.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 9148.

(7) Soundararajan, N.; Platz, M. S.; Jackson, J. E.; Doyle, M. P.; Oon, W.-m.; Liu, M. T. H.; Anand, S. M. *J. Am. Chem. Soc.* **1988**, *110*, 7143.

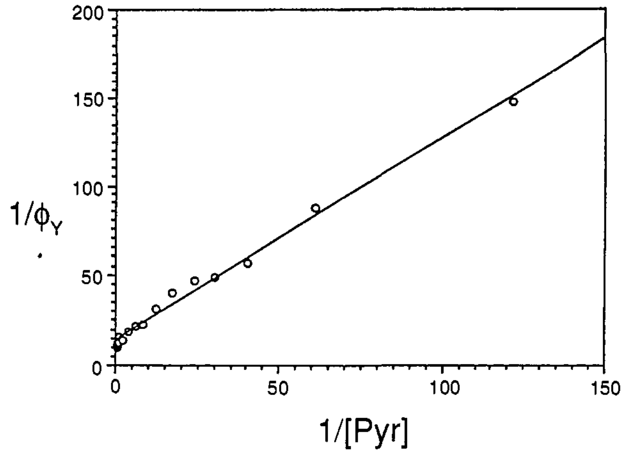

Figure 2. A plot of $1/\phi_y$ versus 1/[pyridine], see text.

attributed to ylide **3**. The spectrum of **3** is similar to those of the other known dialkylpyridine ylides but is somewhat shifted to the blue (364 versus 390–410 nm) of the homocubyl[5] and adamantyl[4] ylides.

The optical yield of ylide **3** is reduced by the presence of oxygen, a selective trap of triplet carbenes.[1,8] From this result two conclusions are possible. The singlet and triplet states of **2** may be of comparable energy, as per aryl- and arylalkylcarbenes, and are in rapid equilibrium.[1] Alternatively a referee has suggested that the excited state of ^{1}**1*** may undergo intersystem crossing to form ^{3}**1*** which extrudes nitrogen to form the triplet carbene.

The intensity of the ylide signal ($\phi_y = \Delta A_{364\text{nm}}$) produced in a laser pulse increases steadily as the concentration of pyridine increases until [PYR] ≈ 1.5 M, at which point the optical yield is saturated. A double reciprocal plot of the data (Figure 2) is linear with a slope of $0.45 = k_T/k_{PYR}K$, where k_{PYR} is the second-order rate constant for reaction of dimethylcarbene with pyridine, K is the equilibrium constant ($K = [2S]/[2T] \ll 1$, assuming the triplet is the ground state as per methylene and that singlet–triplet equilibration is rapid),[9] and k_T is the sum of all first-order and pseudo-first-order rate constants of all processes which consume the carbene in the *absence* of pyridine. These processes include isomerization ($k_{1,2}$) and reaction of the carbene with solvent (k^1_{RH} and k^3_{RH}). Assuming that $k_{PYR}K \approx 10^7$–10^9 s^{-1} [8] pegs the lifetime of the carbene at 1–100 ns in pentane in the *absence* of pyridine. This lifetime must be controlled in part by reaction with solvent because there is a solvent deuterium isotope effect of 1.3 on the slope of plots such as that in Figure 2 in CH_3CN vs CD_3CN and $CHCl_3$ vs $CDCl_3$.

The data convincingly demonstrate that dimethylcarbene is a true reactive intermediate, a species which exists in a potential energy minimum, and has a finite lifetime in solution.

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(8) Sugiyama, M.; Celebi, S.; Platz, M. S. *J. Am. Chem. Soc.* Submitted for publication. The singlet and triplet states of methylene are not in rapid equilibrium in solution;[10] their energy separation is too large.[11]

(9) Scheme I is a conventional[1] interpretation of singlet–triplet phenomena in carbene chemistry. However, it has been pointed out (Griller, D.; Nazran, A. S.; Scaiano, J. *J. Am. Chem. Soc.* **1984**, *106*, 198) that the available data for aryl carbenes is consistent with the presence of a single reactive intermediate, one that can undergo reactions normally ascribed to either the triplet or the singlet state of the carbene. In this interpretation a triplet carbene can react with pyridine to form an ylide via a singlet–triplet surface crossing along the reaction coordinate. The surface crossing mechanism resolves inconsistencies in the kinetics of reaction of triplet diphenylcarbene and methanol. The data of this work is consistent with either a preequilibrium or surface crossing mechanism. The traditional mechanism is presented in Scheme I because there is no compelling reason to discard it with dimethylcarbene.

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

(11) Leopold, D. G.; Murray, K. K.; Miller, A. E. S.; Lineberger, W. C. *J. Chem. Phys.* **1984**, *83*, 4849.

Side-On versus End-On Coordination of Dinitrogen to Titanium(II) and Mixed-Valence Titanium(I)/Titanium(II) Amido Complexes

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Dinitrogen coordination[1] and reduction[2] are among the most challenging of the several transformations (dinitrogen activation,[1,2] reactivity with unsaturated organic substrates,[3] C–H bond activation,[4] CO chemistry,[5] and Ziegler–Natta catalysis[6]) promoted by divalent titanium compounds. Although the great ability of titanocene systems to give dinitrogen fixation with a variety of bonding modes[2] clearly underlines the strength of divalent titanium as a powerful reducing agent; however, the coordination chemistry of the oxidation state +II remains limited to only a few diverse cases.[7,8] To date there are no clearly demonstrated examples where fixation/reduction of dinitrogen occurs on a nonmetallocenic titanium system.

Herein we report the isolation and characterization of two novel dinitrogen Ti(II) and mixed-valence Ti(I)/Ti(II) amido complexes obtained via chlorine replacement at *trans*-(TMEDA)$_2$TiCl$_2$[7e] [TMEDA = *N,N,N′,N′*-tetramethylethylenediamine].

The reaction of *trans*-(TMEDA)$_2$TiCl$_2$ with 1 equiv of (Me$_3$Si)$_2$NLi in toluene under nitrogen at −80 °C formed a purple jelly suspension which turned into a deep-brown solution upon standing overnight at room temperature. Brown crystals of {[(Me$_3$Si)$_2$N]TiCl(TMEDA)}$_2$(μ-N$_2$) (**1**) were obtained after evaporation and crystallization from ether at −30 °C (Scheme I).[9] Occasionally, small amounts of colorless crystals of mo-

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(1) (a) Sanner, R. D.; Duggon, D. M.; McKenzie, T. C.; Marsch, R. E.; Bercaw, J. E. *J. Am. Chem. Soc.* **1976**, *98*, 8358. (b) Pez, G. P.; Armor, N. J. *Adv. Organomet. Chem.* **1981**, *19*, 1. (c) Pez, G. P.; Apgar, P.; Crissey, R. K. *J. Am. Chem. Soc.* **1982**, *104*, 482. (d) Berry, D. H.; Procopio, L. J.; Carroll, P. J. *Organometallics* **1988**, *7*, 570. (e) Flamini, A.; Cole-Hamilton, D. J.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1978**, 454. (f) Busby, R.; Klotzbucher, W.; Ozin, G. A. *Inorg. Chem.* **1977**, *16*, 822.

(2) (a) Van Tamelen, E. *Acc. Chem. Res.* **1970**, *3*, 361. (b) Volpin, M. E.; Shur, V. B.; Kudryavtsev, R. V.; Prodayko, L. A. *J. Chem. Soc., Chem. Commun.* **1968**, 1038. (c) Sobota, P.; Janas, Z. *Inorg. Chim. Acta* **1981**, *53*, L11.

(3) (a) Cohen, S. A.; Auburn, P.; Bercaw, J. E. *J. Am. Chem. Soc.* **1983**, *105*, 1136. (b) Demersman, B.; Coupanec, P. L.; Dixneuf, P. U. *J. Organomet. Chem.* **1985**, *297*, C35. (c) Cohen, S. A.; Bercaw, J. E. *Organometallics* **1985**, *4*, 1006. (d) Sekutowski, D. G.; Stucky, G. D. *J. Am. Chem. Soc.* **1976**, *98*, 1376. (e) Alt, H. G.; Engelhardt, H. E.; Rausch, M. D.; Kool, L. B. *J. Am. Chem. Soc.* **1985**, *107*, 3717. (f) Famili, A.; Farona, M. F.; Thanedar, S. *J. Chem. Soc., Chem. Commun.* **1983**, 435. (g) Green, M. L. H.; Hazel, N. J.; Grebenik, P. D.; Mtetwa, V. S. B.; Prout, K. *J. Chem. Soc., Chem. Commun.* **1983**, 356. (h) Thewalt, U.; Stollmaier, F. *J. Organomet. Chem.* **1982**, *228*, 149.

(4) Bercaw, J. E.; Marvich, R. H.; Bell, L. G.; Britzinger, H. H. *J. Am. Chem. Soc.* **1972**, *94*, 1219.

(5) (a) Kool, L. B.; Rausch, M. D.; Alt, H. G.; Herbershold, M.; Wolf, B.; Thewalt, U. *J. Organomet. Chem.* **1985**, *297*, 159. (b) Frerichs, S. R.; Stein, B. K.; Ellis, J. E. *J. Am. Chem. Soc.* **1987**, *109*, 5558.

(6) (a) Sinn, H.; Kaminsky, W. *Adv. Organomet. Chem.* **1980**, *18*, 99. (b) Boor, J. *Ziegler–Natta Catalysts and Polymerization*; Academic Press: New York, 1979.

(7) Gavens, P. D.; Bottrill, M.; Kelland, J. W.; McMeeking, J. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: New York, 1982.

(8) (a) Jensen, J. A.; Wilson, S. R.; Schultz, A. J.; Girolami, G. S. *J. Am. Chem. Soc.* **1987**, *109*, 8094. (b) Morris, R. J.; Girolami, G. S. *Inorg. Chem.* **1990**, *29*, 4169. (c) Girolami, G. S.; Wilkinson, G.; Galas, A. M. R.; Thornton-Pett, M.; Hursthouse, M. B. *J. Chem. Soc., Dalton Trans.* **1985**, 1339. (d) Durfee, L. D.; Fanwick, P. E.; Rothwell, I. P.; Folting, K.; Huffman, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 4720. (e) Durfee, L. D.; Hill, J. E.; Fanwick, P. E.; Rothwell, I. P. *Organometallics* **1990**, *9*, 75. (f) Edema, J. J. H.; Duchateau, R.; Gambarotta, S.; Hynes, R.; Gabe, E. *Inorg. Chem.* **1991**, *30*, 156. (g) Edema, J. J. H.; Duchateau, R.; Gambarotta, S.; Bensimon, C. *Inorg. Chem.*, in press.

0002-7863/91/1513-8986$02.50/0