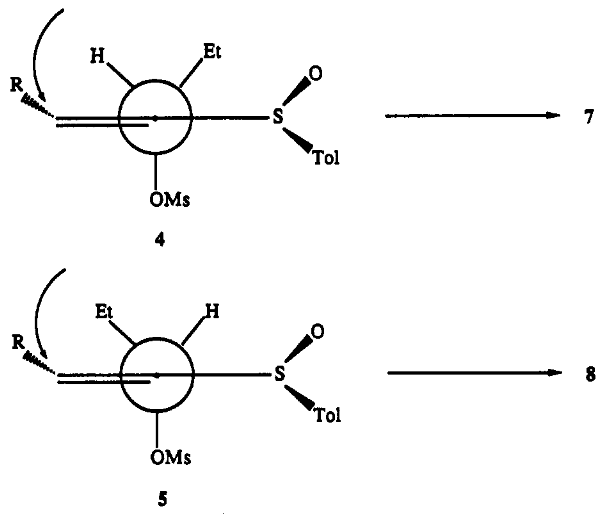
Scheme III



assigned structures were thus confirmed.

The interconversion of diastereomeric alcohols **2a** and **3a** was also examined. While oxidation to the keto sulfoxide proceeded smoothly (MnO_2, CH_2Cl_2, room temperature, 77%), we were unable to effect a clean stereoselective 1,2-reduction under a variety of reaction conditions.[13] However, both isomers could be interconverted via a Mitsunobu protocol[14] followed by debenzoylation (NaOMe, MeOH) in good overall yield (70%).

To extend the scope of the methodology, the introduction of a bulky *tert*-butyl group was addressed and good selectivities were encountered (entries 4 and 5 of Table I). The reactivity of *n*-butyl- and methyl-substituted vinyl sulfoxides **4b,c** and **5b,c**, respectively, prepared as described above from **1b**[15] and **1c**[16] (Scheme I), was also studied, and the results obtained are shown in Table I (entries 6–12). In the case of isomers **4b** and **5b**, excellent yields of displacement adducts were achieved with MeCuCNLi (entries 6, 7). An additional improvement in selectivity for **5b** was encountered when Me_2CuLi was employed (entry 8). In the case of **5c**, high diastereoselectivities were obtained upon reaction with Grignard derived phenyl organocuprates (entries 9, 10). Alternatively, the reactions between diastereomeric mesylate **4c** and *n*-BuCuCNLi and PhCuCNLi proceeded in very good yields and with good stereocontrol.

The above results may be tentatively rationalized in terms of an anti S_N2' process[9,17] on conformation **4** (for diastereomers **4a–c**) and **5** (for diastereomer **5b**)[18] (Scheme III) with oxidative addition of the cuprate opposite to the mesylate and away from the tolyl group. Conformation **5** represents a very delicately balanced case, highly dependent on the reaction conditions and on the steric requirements of the substrate. Thus, when the steric interaction between R and Et group is very strong (R = Ph, **5a**), adduct **9** becomes the main product of the reaction (entry 2), particularly when Grignard derived cuprates are employed (entries 3 and 5).[19] Overall, we feel that the reactions are primarily directed by the allylic mesylate system with the enantioselectivity controlled by the chiral sulfoxide group.

In conclusion, new methodology to effect the regio- and stereocontrolled S_N2' displacement of acyclic allylic mesyloxy vinyl sulfoxides has been developed. In this manner, the newly created chiral carbon center is attached to the synthetically useful functionality of a vinyl sulfoxide. The use of this methodology in synthesis is currently being pursued in our laboratories.

Acknowledgment. This research was supported by the NIH (CA 22237-11) and the C.S.I.C. We thank the Universidad Complutense for a doctoral fellowship to A.V. We thank the Comunidad de Madrid for visiting fellowships to A.V. and R.F.P. We are grateful to Dr. Jeff Kampf for the X-ray analyses of **2a** and **7a**.

Supplementary Material Available: ORTEP drawings, bond angles, and bond distances for compounds **2a** and **7a** and experimental and spectroscopic data for all new compounds (10 pages). Ordering information is given on any current masthead page.

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[12] X-ray data of adduct **7a**: Sulfoxide **7a** crystallized in the orthorhombic space group *Pbc* 2_1, with $a = 7.5133$ (5) Å; $b = 10.96$ (1) Å; $c = 20.175$ (2) Å; and $\beta = 90°$. The structure was solved by direct methods and refined to a $R = 0.0344$ with a final R_w of 0.0518.

[13] DiBAL; DiBAL/$ZnCl_2$; LAH; $NaBH_4/CeCl_3$; LAH/$CeCl_3$; 9-BBN.

[14] Ph_3P, DEAD, $PhCO_2H$, THF, room temperature. See: Grynkiewicz, G.; Burzynska, H. *Tetrahedron* **1976**, *32*, 2109–2111.

[15] Prepared by the method of Kosugi and Uda; see: Kosugi, H.; Kitaoka, M.; Tagami, K.; Takahashi, A.; Uda, H. *J. Org. Chem.* **1987**, *52*, 1078–1082.

[16] Prepared from commercially available 1-bromo-1-propene.

[17] For reviews on S_N2' reactions, see: Marshall, J. A. *Chem. Rev.* **1989**, *89*, 1503–1511. Magid, R. M. *Tetrahedron* **1980**, *36*, 1901–1930.

[18] For a study on the conformation of single vinyl sulfoxides see: Kahn, S. D.; Dobbs, K. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 4602–4606.

[19] At this stage some participation of chelated forms involving the sulfoxide oxygen atom and the mesylate group when Grignard drived cuprates are employed cannot be conclusively ruled out.

A Study of the Kinetics of Diadamantylcarbene in Solution by Laser Flash Photolysis

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Summary: Laser flash photolysis of diadamantyldiazomethane produces diadamantylcarbene which reacts with oxygen to form a carbonyl oxide with λmax = 307 nm.

Recent years have witnessed considerable progress in the study of alkyl substituted carbenes by time resolved techniques.[1] These studies have to date been confined to the study of alkylhalocarbenes by photoacoustic calo-

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[1] (a) Moss, R. A.; Turro, N. J. *Kinetics and Spectroscopy of Carbenes and Biradicals*; Platz, M. S., Ed.; Plenum: New York, 1990; p 213. (b) Platz, M. S.; Maloney, V. M. *Ibid.* p 239.

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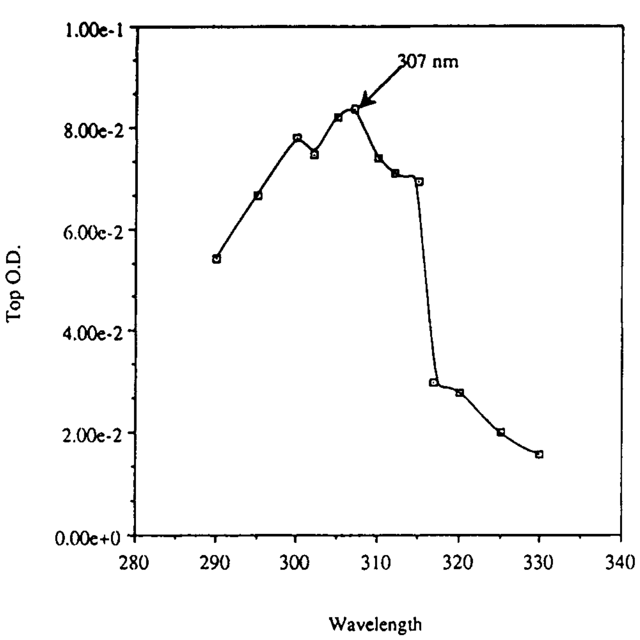
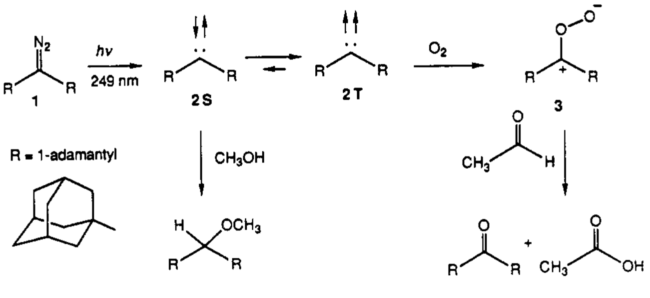


Figure 1. The transient spectrum of carbonyl oxide **3** produced by LFP of **1** in cyclohexane, obtained 200 ns after the laser flash.

Scheme I



rimetry[2] or by laser flash photolysis with UV–vis detection. In the latter technique the ground-state singlet alkylhalocarbenes were monitored by trapping with pyridine to form ylides which absorb intensity around 400 nm.[3] Herein we are pleased to report an extension of the ylide trapping technique to a dialkylcarbene, diadamantylcarbene, which has a triplet ground state.[4]

Laser flash photolysis (LFP) (XeF, 249 nm, 80 mJ, 15 ns) of diadamantyl diazomethane **1** in degassed cyclohexane does not produce a UV–vis active transient intermediate. However, LFP of a flowed, aerated solution of **1** produced the transient spectrum shown in Figure 1, which is attributed to carbonyl oxide **3** (Scheme I). The transient is formed after the flash in an exponential process with a risetime of 200 ns. This lifetime is consistent with the expected, nearly diffusion controlled reaction of a triplet carbene with the low concentration (2.3×10^{-3} M) of oxygen present in solution.[5] The absorption maximum of **3** is blue-shifted by roughly 100 nm relative to benzophenone oxide and other aryl carbonyl oxides because of the lack of conjugation with an aromatic ring, and perhaps because of an increased bond angle at the ylidic carbon due to the steric bulk of the adamantyl groups.[5,6] As expected for a carbonyl oxide, **3** reacts with acetaldehyde ($k = (4.22 \pm 0.35) \times 10^5$ M^{-1} s^{-1}) and pivalaldehyde ($k = (6.90 \pm 2.15) \times 10^5$ M^{-1} s^{-1}).[5,6]

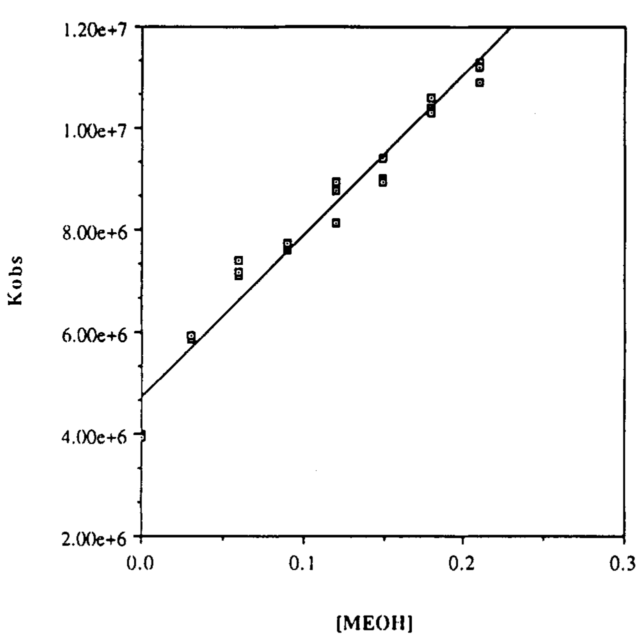


Figure 2. A plot of the observed rate of formation of ylide **3** as a function of methanol concentration.

Scheme I predicts that the yield of **3** will be reduced while its absolute rate of formation will be increased upon LFP of diazo compound **1** in the presence of scavengers of carbene **2**.[7] Both predictions are realized with methanol, which we previously determined was an effective scavenger of singlet diadamantylcarbene **2S**.[4] Stern–Volmer analysis of the methanol quenching data indicates that the absolute rate constant for reaction of the spin-equilibrated carbene with methanol is $(2.0 \pm 0.4) \times 10^7$ M^{-1} s^{-1}. The rate constant of this reaction determined from the slope of a plot of the observed rate constant of carbonyl oxide formation versus [CH_3OH] is $(3.16 \pm 0.81) \times 10^7$ M^{-1} s^{-1}, in reasonable agreement with the Stern–Volmer analysis. Thus diadamantylcarbene and diphenylcarbene ($k = (1\text{–}3) \times 10^7$ M^{-1} s^{-1}),[8] each a ground-state triplet

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(2) (a) LaVilla, J. A.; Goodman, J. L. *J. Am. Chem. Soc.* **1981**, *111*, 712. (b) LaVilla, J. A.; Goodman, J. L. *J. Am. Chem. Soc.* **1989**, *111*, 6877.

(3) (a) Jackson, J. E.; Platz, M. S. *Advances in Chemical Applications of Lasers*; Hilinski, E., Ed.; JAI Press: Greenwich, CT, in press. (b) Jackson, J. E.; Soundararajan, N.; Platz, M. S. *J. Am. Chem. Soc.* **1988**, *110*, 5595. (c) Jackson, J. E.; Soundararajan, N.; Platz, M. S.; Doyle, M. P.; Liu, M. T. H. *Tetrahedron Lett.* **1989**, *30*, 1335. (d) Jackson, J. E.; Soundararajan, N.; White, W.; Liu, M. T. H.; Bonneau, R.; Platz, M. S. *J. Am. Chem. Soc.* **1989**, *111*, 6874. (e) Morgan, S. C. M.S. Thesis, The Ohio State University, 1989. (f) White, W. R.; Platz, M. S.; Chen, N.; Jones, M., Jr. *J. Am. Chem. Soc.* **1989**, *111*, 5973. (g) Bonneau, R.; Liu, M. T. H.; Rayez, M. T. *J. Am. Chem. Soc.* **1989**, *111*, 5973. (h) Ho, G.-J.; Krogh-Jespersen, K.; Moss, R. A.; Shen, S.; Sheridan, R. S.; Subramanian, R. *J. Am. Chem. Soc.* **1989**, *111*, 6875. (i) Liu, M. T. H.; Bonneau, R. *J. Phys. Chem.* **1989**, *93*, 7298. (j) Moss, R. A.; Ho, G.-J.; Shen, S.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1990**, *112*, 1638.

(4) Myers, D. R.; Senthilnathan, V. P.; Platz, M. S.; Jones, M., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 4232.

(5) When two triplet ground state molecules such as **2** and oxygen collide there is a $^1/_9$ probability that they will form a singlet state product as per **3**. Ground-state singlet carbenes such as chlorophenylcarbene do not in general react with oxygen at a measurable rate in solution (ref 3) although the reaction is known to occur in low temperature matrices (ref 6). (a) Werstiuk, N. H.; Casal, H. L.; Scaiano, J. C. *Can. J. Chem.* **1984**, *62*, 2391. (b) Casal, H. L.; Sugamori, S. E. and Scaiano, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 7623. (c) Casal, H. L.; Tanner, M.; Werstiuk, N. H.; Scaiano, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 4616. (d) Barcus, R. L.; Hadel, L. M.; Johnston, L. J.; Platz, M. S.; Savino, T. G.; Scaiano, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 39028. (e) The concentration of oxygen in aerated cyclohexane at 25 °C and 760 mmHg is tabulated in Murov, S. L. *Handbook of Photochemistry*, Dekker: New York, 1973; p 89.

(6) Matrix IR studies of carbonyl oxides indicate that they are best thought of as singlet biradicals. For a recent review; see: Sander, W. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 344.

(7) The pyridine probe method is based upon models developed by Scaiano to probe free radical reactions. For examples, see: (a) Small, R. D., Jr.; Scaiano, J. C. *J. Phys. Chem.* **1977**, *81*, 828. (b) Small, R. D., Jr.; Scaiano, J. C. *Chem. Phys. Lett.* **1977**, *50*, 431. (c) *Ibid.* **1978**, *59*, 246. See also ref 3a.

species, react, at spin equilibrium, with the singlet carbene quencher methanol with about the same rate constant. The absolute rate constant of reaction of trifluoroethanol with diadamantylcarbene is $(1.71 \pm 0.32) \times 10^8$ M^{-1} s^{-1}. The trifluoroethanol rate constant was also found to be 1.51×10^8 M^{-1} s^{-1} by Stern–Volmer analysis in good agreement with the direct method. Triethylsilane reacts with carbene **2** with an absolute rate constant of $(7.33 \pm 2.2) \times 10^6$ M^{-1} s^{-1}. GC–MS analysis of this reaction mixture revealed the formation of diadamantylmethane and hexaethyldisilane as products which shows that it is **2T** rather than **2S** that reacts with triethylsilane.

In summary, oxygen trapping has been used to study the dynamics of a ground-state triplet dialkylcarbene. A previous EPR study deduced that **2T** and triplet diphenylcarbene (DPC) have similar C–C–C bond angles at the carbene carbon.[4,9] The kinetic data demonstrate that **2T** and triplet DPC also react with methanol with comparable rate constants, implying that these two carbenes also have comparable singlet–triplet energy separations.

Acknowledgment. Support of this work by the National Science Foundation (CHE-8814950 Ohio State University, CHE-8800448 Princeton) is gratefully acknowledged.

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(8) (a) Closs, G. L.; Rabinow, B. E. *J. Am. Chem. Soc.* **1976**, *98*, 8196. (b) Eisenthal, K. B.; Turro, N. J.; Sitzmann, E. V.; Gould, J. R.; Hefferon, G.; Langan, J.; Cha, Y. *Tetrahedron* **1985**, *41*, 1543. (c) Griller, D.; Nazran, A. S.; Scaiano, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 198.

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Non-Electron-Transfer Quinone-Mediated Oxidative Cleavage of Cyclopropylamines. Implications Regarding Their Utility as Probes of Enzyme Mechanism[1]

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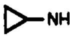
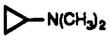
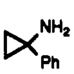
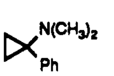
Summary: 3,5-Di-*tert*-butyl-1,2-benzoquinone effects oxidative cleavage of cyclopropylamine (CPA) and its 1-phenyl analogue via *o*-quinoneimine intermediates, a reaction which may serve as a model for the inactivation of plasma amine oxidase by CPA.

Mechanistic diversity in the biological oxidation of amines is an important problem of substantial current research focus. Oxidative ring opening of cyclopropylamines has been a useful mechanistic probe for enzymes thought to oxidize amines by initial one-electron oxidation at nitrogen.[2] Cyclopropylamine (CPA) is also an inactivator[3] of plasma amine oxidase (PAO) a copper-containing enzyme which utilizes a covalently bound quinone cofactor for effecting a pyridoxal-like transamination of primary amines to aldehydes.[4] This cofactor was believed to be pyrroloquinoline quinone (PQQ),[5] but has recently been demonstrated to be the oxidized form of a protein-based 2,4,5-trihydroxyphenylalanine residue.[6] Herein we report on a quinone-mediated oxidative cleavage of cyclopropylamines which is not initiated via one-electron oxidation at nitrogen, and which may serve as a model reaction for investigating the mechanism of copper amine oxidases.

Table I

amine substrate	DTBQ[a] $t_{1/2}$ (h)	$Fe(CN)_6^{3-}$ $t^{1/2}$ (min)[b]
	0.3 (first stage) 38. (second stage)	94.2
	23.	9.0
	12.5	356.
	35.	17.3

[a] $[amine]_o = [DTBQ]_o = 1.25$ mM, 31 °C, pH = 9.0 (2.5 mM carbonate), 50% aqueous CH_3CN; following disappearance of quinone (or quinoneimine) band. [b] Pseudo-first-order conditions; $[amine]_o = 25.0$ mM, $[Fe(III)]_o = 2.5$ mM, [KOH] = 0.5 M, 25 °C; following disappearance of Fe(III).

In exploring preparative methods for the oxidative deamination of amines, Corey and Achiwa[7] found that the Michael-blocked quinone 3,5-di-*tert*-butyl-1,2-benzoquinone (DTBQ) efficiently converted *sec*-alkyl primary amines to ketones.[8] The transamination pathway proposed (Scheme I), involving aromatization to an aminophenol Schiff base, has now been firmly documented for several *o*-quinones.[9-11]

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(1) Presented in preliminary form at the 197th National Meeting of the American Chemical Society, Dallas, April 9–14, 1989, Abstr ORGN 282.

(2) With cytochrome P-450: Macdonald, T. L.; Zirvi, K.; Burka, L. T.; Peyman, P.; Guengerich, F. P. *J. Am. Chem. Soc.* **1982**, *104*, 2050. Hanzlik, R. P.; Tullman, R. H. *J. Am. Chem. Soc.* **1982**, *104*, 2048. With monoamine oxidase: Silverman, R. B. *J. Biol. Chem.* **1983**, *258*, 14766. Silverman, R. B.; Zieske, P. A. *Biochemistry* **1985**, *24*, 2128.

(3) Abeles, R. H. In *Enzyme Activated Irreversible Inhibitors*; Seiler, N., Jung, M. J., Koch-Weser, J., Eds.; Elsevier: Amsterdam, 1978; p 9. We have confirmed that 3 mM CPA results in a 80–85% loss of bovine plasma amine oxidase (Sigma) activity in 30 min at 30 °C.

(4) (a) Farnum, M.; Palcic, M.; Klinman, J. P. *Biochemistry* **1986**, *25*, 1898. (b) Knowles, P. F.; Pandeya, K. B.; Rius, F. X.; Spencer, C. M.; Moog, R. S.; McGuirl, M. A.; Dooley, D. M. *Biochem. J.* **1987**, *241*, 603.

(5) Duine, J. A.; Frank, J.; Jongejan, J. A. *Adv. Enzymol.* **1987**, *59*, 169.

(6) Janes, S. M.; Mu, D.; Wemmer, D.; Smith, A. J.; Kaur, S.; Maltby, D.; Burlingame, A. L.; Klinman, J. P. *Science* **1990**, *248*, 981. Certain other copper amine oxidases appear to contain different protein-based quinone cofactors.

(7) Corey, E. J.; Achiwa, K. *J. Am. Chem. Soc.* **1969**, *91*, 1429.

(8) DTBQ is not useful for converting unbranched primary amines to aldehydes because the initial product **1** is in equilibrium with an oxidizable dihydrobenzoxazole (R^1 = H), giving benzoxazole **2**. We found this oxidation to be mediated by the quinone and not by O_2, as determined by independent synthesis of **1** from 2-amino-4,5-di-*tert*-butylphenol and aldehyde. Such DTBQ-mediated oxidation has been pointed out previously: Vander Zwan, M. C.; Hartner, F. W.; Reamer, R. A.; Tull, R. *J. Org. Chem.* **1978**, *43*, 509.

(9) (a) Eckert, T. S.; Bruice, T. C. *J. Am. Chem. Soc.* **1983**, *105*, 4431. (b) Sleath, P. R.; Noar, J. B.; Eberlein, G. A.; Bruice, T. C. *J. Am. Chem. Soc.* **1985**, *107*, 3328. (c) Rodriguez, E. J.; Bruice, T. C. *J. Am. Chem. Soc.* **1989**, *111*, 7947.

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