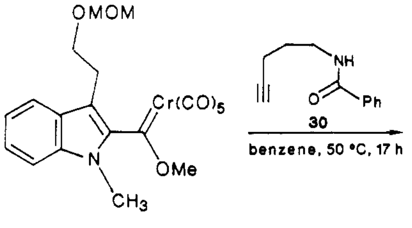
is greater than 350:1. In a similar manner, it was determined that the selectivity for the formation of **23** from the reaction of the complex **11a** was greater than 110:1.

The unexpected finding that the annulations of "ortho"-substituted indolyl carbene complexes give cyclohexadienones of the type **9** rather than the cyclopentadiene **8** permits a consideration of a carbene complex based strategy for entry into a variety of indole alkaloids that would not have been considered in any retroanalysis. The reaction of the carbene complex **29**[6] and the alkyne **30** revealed that these reactions are tolerant of functionality at a level sufficient to prompt our further attention with regard to their development for a totally new approach to the synthesis of *aspidosperma* family of alkaloids of which vindoline **32** is an important member.[16] These findings should also serve to stimulate the investigation of the annulations of other "ortho"-substituted heteroaryl carbene complexes.



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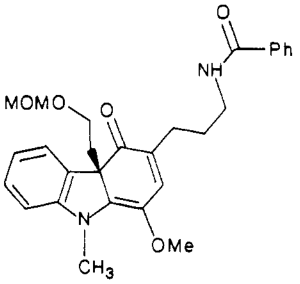
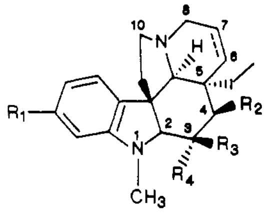


31 59%



32 vindoline R_1 = OMe, R_2 = OAc, R_3 = OH, R_4 = CO_2Me

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Supplementary Material Available: Spectral data for all new compounds (9 pages). Ordering information is given on any current masthead page.

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[16] For reviews, see: (a) Saxton, J. E. *Nat. Prod. Rep.* **1987**, *4*, 591. (b) Overman, L. E.; Sworin, M. In *Alkaloids, Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1985; Vol. 3, p 275. (c) Cordell, G. A. In *The Alkaloids*; Manske, R. H. F., Rodrigo, R. G. A., Eds.; Academic Press: New York, 1979; Vol. XVII, p 199. For citations, see: (d) Magnus, P.; Gallagher, T.; Brown, P.; Pappalardo, P. *Acc. Chem. Res.* **1984**, *17*, 35. For recent citations, see: (e) Feldman, P. L.; Rapoport, H. *J. Am. Chem. Soc.* **1987**, *109*, 1603. (f) Node, M.; Nagasawa, H.; Fuji, K. *J. Am. Chem. Soc.* **1987**, *109*, 7901. (g) Kuehne, M. E.; Zebovitz, T. C. *J. Org. Chem.* **1987**, *52*, 4331. (h) Brennan, J. P.; Saxton, J. E. *Tetrahedron* **1987**, *43*, 191. (i) Cardwell, K.; Hewitt, B.; Ladlow, M.; Magnus, P. *J. Am. Chem. Soc.* **1988**, *110*, 2242. (j) Hugel, G.; Pfeuffer, L. *Tetrahedron Lett.* **1987**, *28*, 1773. (k) Ogawa, M.; Kitagawa, Y.; Natsuma, M. *Tetrahedron Lett.* **1987**, *28*, 3985. (l) Jackson, A. H.; Shannon, P. V. R.; Wilkens, D. J. *Tetrahedron Lett.* **1987**, *28*, 4901.

A New Oxidizing Reagent: Triethylsilyl Hydrotrioxide

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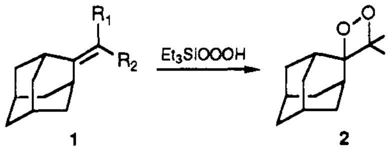
Summary: Triethylsilyl hydrotrioxide ($Et_3SiOOOH$) is a new, short-lived oxidizing agent that can react at −78 °C directly and rapidly with olefins to form 1,2-dioxetanes and oxidatively cleaved carbonyl products.

Sir: Triethylsilyl hydrotrioxide ($Et_3SiOOOH$), prepared in situ at −78 °C in CH_2Cl_2 from triethylsilane plus ozone, was reported in 1986 to be a new chemical source of the powerful oxidant singlet molecular oxygen ($^1O_2$).[1] Shortly thereafter we showed for the first time (1) a *direct* reaction of $Et_3SiOOOH$ (i.e., not via free $^1O_2$) with some electron-rich arylalkenes and (2) the superiority of $Et_3SiOOOH$ over free $^1O_2$ for preparation of an aryldioxetane.[2] Herein (1) $Et_3SiOOOH$ is shown to react within seconds at −78 °C directly also with *unactivated olefins* to form oxidatively cleaved carbonyl products, and (2) a dioxetane is isolated for the first time from direct reaction of $Et_3SiOOOH$ with an *electron-rich olefin.*

A precooled (−78 °C) methylene chloride solution of the electron-rich tetrasubstituted enol ether **1a**[3] was added immediately and rapidly via cannula to a large excess of very freshly prepared $Et_3SiOOOH$ in methylene chloride at −78 °C.[1] After a few minutes, product isolation by preparative TLC gave dioxetane **2a** in 47% yield, having ^1H NMR signals at δ 3.05 and 2.22 and a mass spectrum characteristic of an authentic sample of dioxetane **2a**.[3] In



(1)

	R_1	R_2	yield, %
a	OMe	*m*-HOC_6H_4	47
b	OMe	H	34
c	H	C_6H_5	–

[†] Department of Chemistry.

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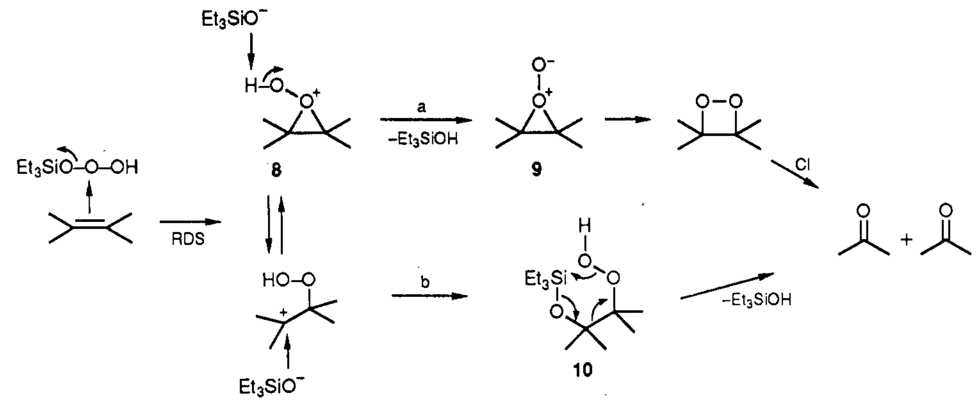
[1] Corey, E. J.; Mehrotra, M. M.; Khan, A. U. *J. Am. Chem. Soc.* **1986**, *108*, 2472.

[2] Posner, G. H.; Weitzberg, M.; Nelson, W. M.; Murr, B. L.; Seliger, H. H. *J. Am. Chem. Soc.* **1987**, *109*, 278.

[3] We thank Drs. Brooks Edwards and Irena Bronstein of Quest Systems Inc. for a generous gift of enol ether **1a** and for the ^1H NMR spectrum of authentic dioxetane **1c**. See: Bronstein, I.; Edwards, B.; Voyta, J. C. *J. Bioluminescence Chemiluminescence* **1988**, *2*, 186. See also: Bronstein, I.; McGrath, P. *Nature* **1989**, *338*, 599.

0022-3263/89/1954-3252$01.50/0

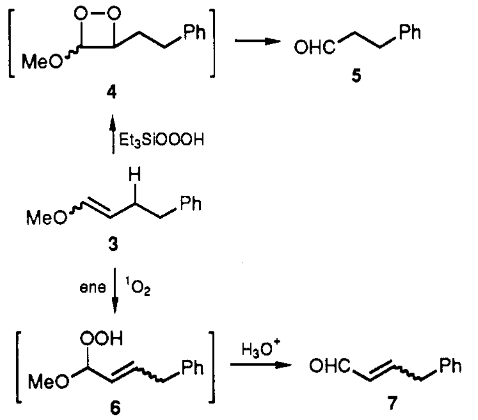
Scheme I



separate controls, dioxetane **2a** was found to be stable to ozone and to prolonged exposure to $Et_3SiOOOH$ (i.e., stable to Et_3SiOH and $^1O_2$). Similar treatment[4a] of the electron-rich trisubstituted enol ether **1b**[4b,c] produced intermediate dioxetane **2b**, which was reduced by excess lithium aluminum hydride added after 5 or 20 s at −78 °C to form the corresponding diol,[5] 2-(2-(hydroxymethyl))-adamantanol, as the major product isolated in the same yield from both the 5- and 20-s reactions along with some unreacted enol ether **1b**. At −78 °C in CH_2Cl_2, with the half-life of $Et_3SiOOOH$ toward release of free $^1O_2$ being much greater than 150 s,[1] dioxetane formation must have occurred at least to a large degree via reaction of enol ether **1b** *directly* and immediately with $Et_3SiOOOH$. In contrast, treatment of styrenyl adamantane **1c** with fresh $Et_3SiOOOH$ and then immediately with $LiAlH_4$ gave only a trace of a diol along with 2-adamantanol and benzyl alcohol as the major products.

To rule out free ozone, which was used to generate triethylsilyl hydrotrioxide from triethylsilane, as the major oxidant generally in $Et_3SiOOOH$ reactions and specifically in reaction of styrenyl system **1c**, the following evidence is provided: (1) the ratio of Et_3SiH:O_3 was 2:1 to avoid the presence of any free O_3; (2) the deep blue color of the ozone-saturated methylene chloride solution disappeared within seconds after addition of Et_3SiH; and (3) control experiments under the same reaction conditions but with exclusion of Et_3SiH (i.e., an ozone-saturated methylene chloride solution at −78 °C) caused formation of ozonolysis products in only about 10–15% yields.

As further evidence that $Et_3SiOOOH$ can react as a discrete oxidizing (e.g., dioxetane-forming) reagent different from free $^1O_2$, a precooled (−78 °C) CH_2Cl_2 solution of electron-rich disubstituted enol ether **3**[4c] was added immediately and rapidly via cannula to a large excess of freshly prepared triethylsilyl hydrotrioxide in CH_2Cl_2 at −78 °C, producing mainly intermediate dioxetane **4**, which, upon warming, underwent cleavage into aldehyde **5**, isolated as the corresponding alcohol (3-phenylpropanol) in 44% yield after lithium aluminum hydride reduction (eq 2). In sharp contrast, the same enol ether **3** reacted with $^1O_2$ (generated photochemically)[6] primarily via an ene pathway forming intermediate allylic hydroperoxide **6**, which was isolated as its hydrolysis product **7** in 37% yield (eq 2).



(2)

The terminal, *unactivated* olefin allylbenzene reacted with fresh triethylsilyl hydrotrioxide and then with lithium aluminum hydride to form 2-phenylethanol in 47% yield. This oxidative cleavage of allylbenzene by $Et_3SiOOOH$ is especially noteworthy in this case where $^1O_2$ is expected to enter into an ene allylic oxidation with rupture of a relatively weak benzylic C–H bond and formation of a conjugated styrene unit in the product allylic hydroperoxide.[6] Furthermore, whereas $^1O_2$ is known to react exclusively via an ene process with terminal monosubstituted aliphatic alkenes[7] and with internal disubstituted aliphatic alkenes,[8] fresh triethylsilyl hydrotrioxide reacted with methyl oleate followed by lithium aluminum hydride to produce 1-nonanol and 1,9-nonanediol in 64 and 74% yields, respectively (eq 3).

$$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOMe \xrightarrow{Et_3SiOOOH} CH_3(CH_2)_7CHO + OCH(CH_2)_7COOMe \quad (3)$$

A dioxetane was not the major intermediate when 2-phenyl-1-hexene was added to fresh $Et_3SiOOOH$ at −78 °C in CH_2Cl_2; valerophenone was the major product. If a dioxetane intermediate had been formed in this case,

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(4) (a) Enol ether **1b** was allowed to react with 12 equiv of fresh triethylsilyl hydrotrioxide; (b) prepared via Wittig methoxymethylenation of adamantanone; (c) all new compounds were characterized spectroscopically and by mass spectral or combustion analysis.

(5) For general review of preparation and reactions of 1,2-dioxetanes, see: (a) *Chemical and Biological Generations of Excited States*; Adam, W., Cilento, G., Eds.; Academic: New York, 1982. (b) Adam, W. In *The Chemistry of Functional Groups, Peroxides*; Patai, S., Ed.; Wiley: New York, 1983. (c) Adam, W.; Baader, W. J.; Babatsikos, C.; Schmidt, E. *Bull. Soc. Chim. Belg.* **1984**, *93*, 605. (d) Adam, W.; Yang, F. *In Small Ring Heterocycles*, Hassner, A., Ed.; Wiley: New York, 1985; Part 3, Chapter 4.

(6) For reviews of $^1O_2$ chemistry, see: (a) Denny, R. W.; Nickon, A. *Org. React.* (*N.Y.*) **1973**, *20*, 133; (b) *Singlet Oxygen*; Wasserman, H. H., Murray, R. W., Eds.; Academic: New York, 1979. (c) *Singlet O_2*; Frimer, A., Ed.; CRC: Boca Raton, FL, 1985. See also: Sugimoto, S.; Sawyer, D. T.; Kanofsky, J. R. *J. Am. Chem. Soc.* **1988**, *110*, 8707.

(7) Kopecky, K.; Reich, H. *Can. J. Chem.* **1965**, *43*, 2265.

(8) (a) Cobern, D.; Hobbs, J. S.; Lucas, R. A.; Mackenzie, D. J. *J. Chem. Soc. C* **1966**, 1897. (b) Hall, G. E.; Roberts, D. G. *J. Chem. Soc. B* **1966**, *1109*.

then triplet excited state valerophenone would have been produced, leading via a Norrish type II cleavage[9] to some acetophenone; no acetophenone was detected by capillary GLPC using authentic standards. Although this failure to detect a dioxetane intermediate as well as that involving styrenyl system **1c** do not prove necessarily that no dioxetane is involved, taken together they suggest strongly that oxidative cleavage of unactivated olefins by $Et_3SiOOOH$ proceeds *mainly* via a nondioxetane pathway.

To account for $Et_3SiOOOH$ acting with electron-rich olefins (e.g., enol ethers) as a dioxetane-forming reagent and with unactivated olefins as a non-dioxetane carbonyl-forming reagent, the mechanism shown in Scheme I is tentatively proposed. This mechanism involves electrophilic $Et_3SiOOOH$[10] undergoing nucleophilic attack by the π-electrons of an olefin with loss of a siloxide ion producing positively charged species having carbocation and/or oxonium ion character; oxonium ion **8** is a protonated perepoxide which can undergo deprotonation via pathway a to produce intermediate perepoxide **9**.[5] Such perepoxides are widely discussed intermediates thought to produce dioxetanes and ultimately two carbonyl cleavage products along with chemiluminescence (CL).[5] Consistent with the intermediacy of perepoxides, some epoxide was indeed observed during $Et_3SiOOOH$ reaction with enol ether **1b**. This mechanistic pathway has some analogy to a mechanism for peracid epoxidation of olefins (i.e., epoxonium ion intermediate).[11] Alternatively, siloxide ion nucleophilic attack at a cationic carbon atom of the initial positively charged intermediate can lead, via pathway b, to *vicinal* peroxy glycol **10**; facile loss of Et_3SiOH with concomitant scission of the glycol unit into two *ground-state* carbonyl fragments would produce neither dioxetanes nor CL. Because *homolysis* of weak peroxidic bonds is a relatively easy process,[5,12] Scheme I could involve radical rather than ionic intermediates.

The results reported here demonstrate for the first time (1) oxidative cleavage of *unactivated olefins* into carbonyl fragments via direct reaction with fresh $Et_3SiOOOH$ (i.e., not via free $^1O_2$ or free O_3) and (2) conclusive evidence for dioxetanes as the major intermediates from direct reaction of nonaromatic *electron-rich olefins* with fresh $Et_3SiOOOH$. These findings raise many mechanistic questions (e.g., ionic and/or radical pathways[13,14]) and synthetic possibilities that we are pursuing.

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Supplementary Material Available: Experimental procedure for oxidative cleavage of methyl oleate (1 page). Ordering information is given on any current masthead page.

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[9] (a) Turro, N. J.; Dalton, J. C.; Dawes, K.; Farrington, G.; Hautala, R.; Morton, D.; Niemczyk, M.; Schore, N. *Acc. Chem. Res.* **1972**, *5*, 92. (b) Wagner, P. J. *Ibid.* **1971**, *4*, 168. (c) For a specific example of formation of acetophenone from a valerophenone triplet derived from a dioxetane, see: Turro, N. J.; Chow, M.-F. *J. Am. Chem. Soc.* **1980**, *102*, 5058.

[10] (a) For a review of silyl hydrotrioxides, see: Aleksandrov, Yu. A.; Tarunin, B. I. *Russ. Chem. Rev. (Engl. Transl.)* **1977**, *46*, 905. (b) For generation of dioxetanes via ozonolysis of vinylsilanes, see: Büchi, G.; Wüest, H. *J. Am. Chem. Soc.* **1978**, *100*, 294. Avery, M. A.; Jennings-White, C.; Chong, W. K. M. *Tetrahedron Lett.* **1987**, *28*, 4629; *J. Org. Chem.* **1989**, *54*, 1789.

[11] Hanzlik, R. P.; Shearer, G. O. *J. Am. Chem. Soc.* **1975**, *97*, 5231 and references therein. See also: Plesnicar, B. In *The Chemistry of Functional Groups, Peroxides*; Patai, S., Ed.; Wiley: New York, 1983; pp 521-584.

[12] Cf.: Spialter, L.; Pazdernik, L.; Bernstein, S.; Swansiger, W. A.; Buell, G. R.; Freeburger, M. E. *Adv. Chem. Ser.* **1972**, *No. 112*, 65.

[13] Nelson, S. F. *Acc. Chem. Res.* **1987**, *20*, 269.

[14] Plesnicar, B.; Kovac, F.; Schara, M. *J. Am. Chem. Soc.* **1988**, *110*, 217 and references therein.

Synthesis and Consecutive Double Alkylation Reactions of (2-Siloxyallyl)silanes as the Synthetic Equivalent of Acetone α,α'-Dianion[1]

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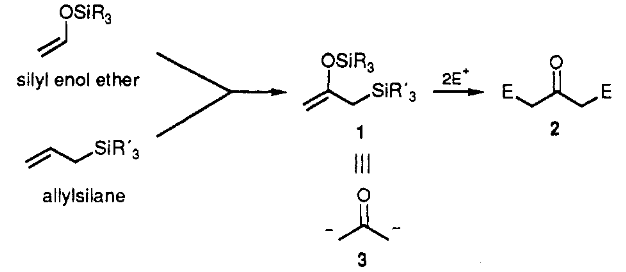
Received February 27, 1989

Summary: (2-Siloxyallyl)silanes as the synthetic equivalent of tandem acetone α,α'-dianion, readily prepared by quenching of the enolate of α-(trimethylsilyl)acetone with chlorosilanes or by 1,3 C→O Si shift of bis(organosilyl)acetone, react with various electrophiles promoted by a Lewis acid to give the corresponding α,α'-disubstituted acetones.

Sir: Much attention has been focused on the application of organosilicon compounds as synthetic equivalents of reactive intermediates, otherwise inaccessible.[2] Especially allylsilanes and silyl enol ethers are versatile reagents in organic synthesis and have vast potential as a variety of

Scheme I. (2-Siloxyallyl)silane (1) as Acetone α,α'-Dianion Synthon (3)



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[1] Studies on Organosilicon Chemistry. 98. For 97, see: Hayashi, T.; Matsumoto, Y.; Kiyoi, T.; Ito, Y.; Kohra, S.; Tominaga, Y.; Hosomi, A. *Tetrahedron Lett.* **1988**, *29*, 5667. For 96, see: Hosomi, A.; Kohra, S.; Tominaga, Y. *Chem. Pharm. Bull.* **1988**, *36*, 4622. For 95, see: Hosomi, A.; Ogata, K.; Hoashi, K.; Kohra, S.; Tominaga, Y. *Ibid.* **1988**, *36*, 3736. For 94, see: Tominaga, Y.; Matsuoka, Y.; Hayashida, H.; Kohra, S.; Hosomi, A. *Tetrahedron Lett.* **1988**, *29*, 5771.

[2] (a) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981. (b) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983. Fleming, I. *Chem. Soc. Rev.* **1981**, *10*, 83.