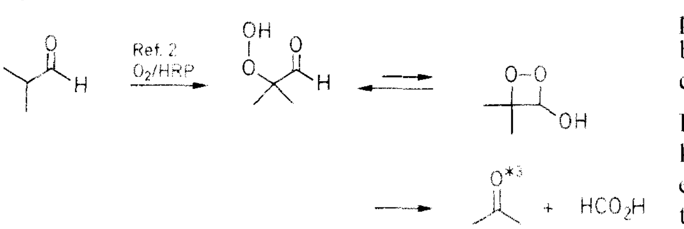
Synthesis of Trialkylsilylated α-Hydroperoxy Aldehydes and Ketones via Ozonolysis of Protected Allylic Hydroperoxides

Waldemar Adam,* Luiz H. Catalani,[1] Chantu R. Saha-Möller, Bernd Will

Institute of Organic Chemistry, University of Würzburg, D-8700 Würzburg, Federal Republic of Germany

α-Silylperoxy aldehydes and ketones **3** have been prepared by ozonolysis of silyl-protected allylic hydroperoxides, followed by subsequent reduction of the latter with dimethyl sulfide. Deprotection of silylperoxy aldehydes **3a–c** with fluoride ion led to decomposition with chemiluminescence.

In the horse radish peroxidase (HRP) catalyzed autoxidation of isobutyraldehyde affording acetone in a triplet excited state, 3-hydroxy-1,2-dioxetanes were postulated as intermediates. Cyclization of the intermediary α-hydroperoxy aldehyde leads to its cyclic tautomer, which as a labile species is expected to fragment via a chemical excitation into triplet acetone and the formate ion, the former manifesting itself through chemiluminescence.[3]



Since to date no α-hydroperoxy aldehydes appear to have been isolated to substantiate the above mechanistic claim, we attempted to prepare stable derivatives and confirm their role as chemiluminescent precursors. In view of the anticipated labile nature of the α-hydroperoxy aldehydes, we decided to prepare trialkylsilylated derivatives via the sequence outlined below, releasing the free substances by mild desilylation at the moment of need.

The allylic hydroperoxides **1** that are required as starting materials were prepared by conventional photooxygenation[5] and are all known. For the silylation[4,6] to the silylperoxy derivatives **2**, we preferred *tert*-butyldimethylsilyl chloride because of the higher hydrolytic stability of the subsequent products (Table 1). Ozonolysis in methanol at −78 °C followed by dimethyl sulfide reduction led to the α-silylperoxy carbonyl compounds **3** in moderate to good yields (Table 2).

Desilylation by methanol of α-silylperoxy ketone **3e** afforded the known 2-hydroperoxy-2-methylbutanone, which was independently prepared by base-catalyzed autoxidation of 3-methylbutan-2-one.[7] However, for the α-silylperoxy aldehydes **3a–c**,

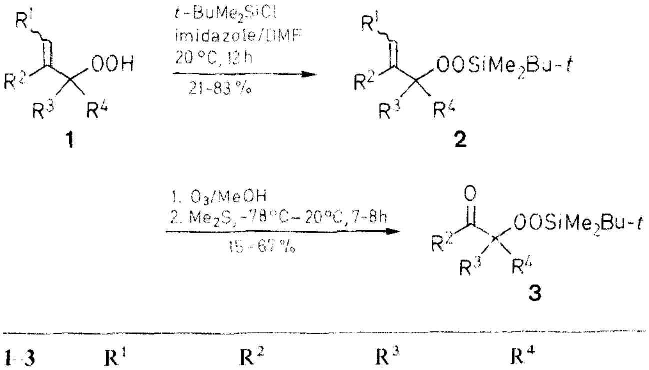
Table 1. Allylic *tert*-Butyldimethylsilyl Peroxides **2** Prepared

Product	Yield[a] (%)	Molecular Formula[b]	IR (neat or CCl_4) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[c] δ, *J* (Hz)	^{13}C-NMR ($CDCl_3$/TMS)[d] δ
2a	21	$C_{10}H_{22}O_2Si$ (202.4)	3160, 3090, 2960, 2930, 2890, 2860, 1640, 1470, 1460, 1255, 1250 (s, SiOO), 1140, 1050, 990, 870	0.15 (s, 6H, $(CH_3)_2$); 0.92 (s, 9H, $C(CH_3)_3$); 1.25 (d, 3H, *J* = 6.4); 4.42 (dddq, 1H, *J* = 6.4, 6.9, 1.0, 1.2); 5.16 (ddd, 1H, *J* = 10.2, 1.4, 1.0); 5.23 (ddd, 1H, *J* = 17.2, 1.4, 1.2); 5.83 (ddd, 1H, *J* = 17.2, 10.2, 6.9)	−5.6 (q); 18.2 (s); 18.25 (q); 26.2 (q); 82.2 (d); 116.8 (t); 138.3 (d)
2b	48	$C_{12}H_{26}O_2Si$ (230.4)	2970, 2935, 2882, 2860, 1670, 1470, 1460, 1365, 1255, 1250 (s, SiOO), 965, 880, 840, 785	0.15 (s, 6H, $(CH_3)_2$); 0.89 (t, 3H, CH_2CH_3, *J* = 7.5); 0.94 (s, 9H, $(CH_3)_3$); 1.46 (ddq, 1H, CH_ACH_3, *J* = 15.0, 7.5); 1.71 (ddq, 1H, CH_BCH_3, *J* = 15.0, 7.5, 5.7); 1.73 (dd, 3H, $C=CCH_3$, *J* = 6.6, 1.7); 4.13 (ddt, 1H, CH–OOSi, *J* = 0.6, 8.2, 5.7); 5.38 (ddq, 1H, *J* = 1.7, 15.3, 8.2); 5.7 (ddq, 1H, *J* = 6.6, 15.3, 0.6)	−5.6 (q); 9.7 (q); 17.8 (q); 18.2 (s); 25.7 (t); 25.9 (q); 87.8 (d); 130.0 (d); 130.2 (d)
2c	72[e]	$C_{11}H_{24}O_2Si$ (216.4)	3090, 2960, 2935, 2900, 2860, 1650, 1470, 1460, 1360, 1255, 1250 (s, SiOO), 1140, 1080, 905	0.15 (s, 6H); 0.94 (s, 9H); 1.31 (s, 6H); 5.06 (dd, 1H, *J* = 1.2, 11.0); 5.16 (dd, 1H, *J* = 1.2, 17.7); 6.0 (dd, 1H, *J* = 11.0, 17.7)	−5.5 (q); 18.3 (s); 24.3 (q); 26.3 (q); 82.2 (s); 113.4 (t); 142.9 (d)
2d	66[e]	$C_{11}H_4O_2Si$ (216.4)	3095, 2965, 2940, 2900, 2865, 1655, 1475, 1465, 1370, 1250 (s, SiOO), 1145, 1080, 910	0.15 (s, 6H); 0.94 (s, 9H); 1.10 (d, 3H, *J* = 6.5); 1.59 (dd, 3H, $C=CCH_3$, *J* = 1.4, 1.0); 4.26 (q, 1H, CH–OOSi, *J* = 6.5); 4.73 (m, 1H); 4.78 (m, 1H)	−5.7 (q); 13.4 (q); 17.5 (q); 18.2 (s); 26.2 (q); 84.6 (d); 112.6 (t); 145.1 (s)
2e	83	$C_{12}H_{26}O_2Si$ (230.4)	3100, 2960, 2890, 2860, 1640, 1470, 1460, 1370, 1360, 1255, 1250 (s, SiOO), 1150, 1090, 900	0.12 (s, 6H); 0.92 (s, 9H); 1.30 (s, 6H); 1.78 (m, 3H); 4.83 (m, 1H); 4.89 (m, 1H)	−5.6 (q); 18.7 (s); 24.2 (q); 25.7 (q); 26.3 (q); 83.8 (s); 110.6 (t); 149.4 (s)

[a] Yield of the analytically pure product based on hydroperoxide **1**.
[b] Satisfactory microanalyses obtained: C ±0.14, H ±0.22.
[c] Recorded on a Bruker WM-400 (400 MHz) spectrometer.
[d] Recorded on a Bruker AC200 (50 MHz) or WM-400 (100 MHz) spectrometer.
[e] A 1:1 mixture of allyl hydroperoxides **1c** and **1d** was used in the silylation, but the yields are based on 100% of each of the corresponding hydroperoxides.

desilylation with methanol gave the hemiacetals, which were detected by means of ^{1}H-NMR spectroscopy. Attempts to extrude methanol from these led to decomposition. Fluoride ion catalyzed deprotection also gave decomposition, but with chemiluminescence. Presumably the intermediary α-peroxy anion cyclized (precedents are known[8]) to the labile dioxetane and cleavage afforded the electronically excited carbonyl compound with subsequent light emission. Although it was still not possible to isolate stable α-hydroperoxy aldehydes, the results make their intermediacy seem plausible.

Commercial grade reagents and solvents were used without further purification, except when indicated. Infrared spectra were obtained by using Perkin-Elmer 1420 spectrophotometer. Elemental analyses were performed either in-house or at the Microanalysis Laboratories of the University of Giessen (FRG). We thank Prof. Dr. G. Maier and his staff for this service. Mass spectra were recorded on a Finnigan MAT 8200 spectrometer at 80 eV. Melting points and boiling points are uncorrected. The qualitative chemiluminescence experiments of the fluoride ion promoted deprotection of the silylperoxy aldehydes **3a–c** was performed using the apparatus and method described previously.[9]



1–3	R^1	R^2	R^3	R^4
a	H	H	H	CH_3
b	CH_3	H	H	CH_3CH_2
c	H	H	CH_3	CH_3
d	H	CH_3	H	CH_3
e	H	CH_3	CH_3	CH_3

Photooxygenation of Alkenes to Form Allylic Hydroperoxides 1; General Procedure:

The starting alkene (20 mmol) is dissolved in CH_2Cl_2 (20 mL) containing tetraphenylporphin (2–5 mg) as sensitizer. The mixture is irradiated with a sodium street lamp (Phillips G/98/2 SON 150 Watt) at −5 °C, while a slow stream of dry oxygen gas is passed through. The reaction is monitored by ^{1}H-NMR spectroscopy and/or TLC. After completion (2–4 d), the solvent is removed on a rotary evaporator (0 °C/20 Torr), and the residue is fractionally distilled at reduced pressure.

Allylic *tert*-Butyldimethylsilyl Peroxides 2; General Procedure:

In a flame-dried, 50-mL, three-necked, round-bottomed flask containing a solution of *tert*-butyldimethylsilyl chloride (1.8 g, 12 mmol) and imidazole (0.95 g, 14 mmol) in DMF (50 mL, freshly distilled from CaH_2) is added the hydroperoxide **1** (10 mmol) under a nitrogen atmosphere. For **1a** and **1b** imidazole is replaced by diisopropylmethylamine (1.8 g, 12 mmol) and *N,N*-dimethylaminopyridine (6.0 mg, 0.4 mmol). The reaction mixture is stirred at 20 °C for 12 h (for **2c** and **2d** 2h), diluted with ether (50 mL), quickly washed with 1 N aq. HCl (40 mL) and with sat. aq. $NaHCO_3$ (40 mL), and dried (Na_2SO_4). The solvent is removed by rota-evaporation (0 °C/20 Torr) and the residue is purified by flash chromatography (SiO_2, hexane/CH_2Cl_2, 1:1, 20 °C).

2-Oxoalkyl *tert*-Butyldimethylsilyl Peroxides 3; General Procedure:

Silyl peroxide **2** (2 mmol) is dissolved in absolute MeOH (20 mL), cooled to −78 °C. A gentle stream of dry ozone is allowed to pass through the solution until the characteristic blue ozone color persists.

Table 2. α-Silylperoxy Carbonyl Compounds **3** Prepared

Product	Yield[a] (%)	Molecular Formula[b] or MS (DCI, 80 eV) *m/z* (%)	IR (neat or CCl_4) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[c] δ, J (Hz)	^{13}C-NMR ($CDCl_3$/TMS)[d] δ
3a	15	222 (100, $M^+ + 18$)	2960, 2930, 2860, 1735 (s, C=O), 1470, 1460, 1375, 1360, 1255, 1250 (s, SiOO)	0.20 (s, 6H); 0.97 (s, 9H); 1.23 (d, 3H, $J = 6.1$); 4.29 (dq, 1H, $J = 6.1, 3.0$); 9.80 (d, 1H, $J = 3.0$)	−5.9 (q); 12.9 (q); 18.1 (s); 26.0 (q); 84.9 (d); 203.1 (d)
3b	23	236 (100, $M^+ + 18$)	2960, 2935, 2890, 2860, 2820, 1740 (s, C=O), 1470, 1460, 1365, 1255, 1250 (s, SiOO), 880	0.18 (s, 3H, $SiCH_3$); 0.20 (s, 3H, $SiCH_3$); 0.94 (s, 9H, $(CH_3)_3$); 1.0 (t, 3H, $CH_2\underline{CH_3}$, $J = 7.5$); 1.66 (dq, 2H, $\underline{CH_2}CH_3$, $J = 7.5, 6.8$); 4.10 (dt, 1H, CH–OOSi, $J = 6.8, 3.2$); 9.77 (d, 1H, $J = 3.2$)	−5.9 (q); 9.4 (q); 18.2 (s); 21.5 (t); 26.0 (q); 90.1 (d); 203.5 (d)
3c	24	$C_{10}H_{22}O_3Si$ (218.4)	2960, 2940, 2900, 2860, 1740 (s, C=O), 1475, 1465, 1385, 1365, 1260, 1255 (s, SiOO), 1175	0.16 (s, 6H); 0.92 (s, 9H); 1.27 (s, 6H); 9.70 (s, 1H)	−5.7 (q); 18.2 (s); 19.4 (q); 26.1 (q); 86.5 (s); 203.2 (d)
3d	25	$C_{10}H_{22}O_3Si$ (218.4)	2960, 2930, 2895, 2858, 1725 (s, C=O), 1470, 1460, 1355, 1250 (s, SiOO), 1145, 1090, 862	0.14 (s, 3H); 0.16 (s, 3H); 0.91 (s, 9H); 1.22 (d, 3H, $J = 7.0$); 2.26 (s, 3H); 4.27 (q, 1H, $J = 7.0$)	−5.9 (q); 14.7 (q); 18.1 (s); 24.3 (q); 26.0 (q); 86.2 (d); 210.9 (s)
3e	67	$C_{11}H_{24}O_3Si$ (232.4)	2960, 2930, 2890, 2860, 1715 (s, C=O), 1470, 1460, 1375, 1360, 1350, 1255, 1250 (s, SiOO), 1215, 1165, 1130, 845	0.17 (s, 6H); 0.93 (s, 9H); 1.29 (s, 6H); 2.27 (s, 3H)	−5.7 (q); 18.2 (s); 21.4 (q); 23.9 (q); 26.1 (q); 87.9 (s); 211.4 (s)

[a] Yield of the analytically pure product based on **2**.

[b] Satisfactory microanalyses obtained: C ±0.33, H ±0.15.

[c] Recorded on a Bruker WM-400 (400 MHz) spectrometer.

[d] Recorded on a Bruker AC200 (50 MHz) or WM-400 (100 MHz) spectrometer.

The excess ozone is removed by purging the reaction mixture with dry nitrogen gas, and dimethyl sulfide (2 mL) is added at −78 °C. The resulting solution is warmed to 20 °C and stirred for 7–8 h. The solvent is removed on a rotary evaporator (0 °C/20 Torr), and the residue is purified by means of flash chromatography (SiO_2, hexane/CH_2Cl_2, 1:1, −20 °C).

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(1) A. v. Humboldt postdoctoral fellow 1984–86; present address: Department of Fundamental Chemistry, University of Sao Paulo, Cidade Universitaria, Caixa Postal 20.780, Sao Paulo, Brasil.

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