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1,2-Dioxetanes from Vinyl Aromatics

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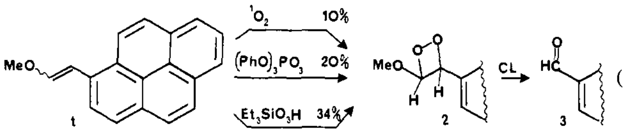
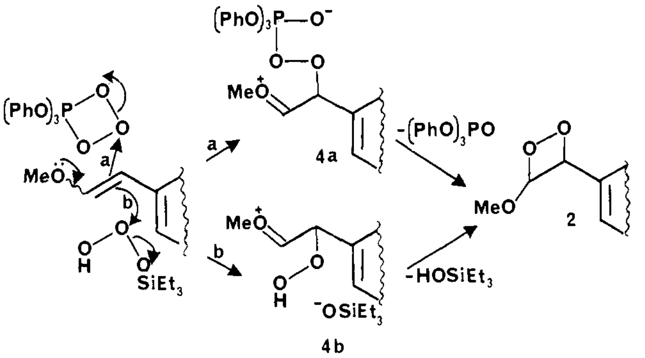
Aryldioxetanes are usually difficult to prepare via direct dioxygenation of 1-arylalkenes.[1] Singlet molecular oxygen ($^{1}O_2$) generated chemically (NaOCl + H_2O_2) or photochemically ($^{3}O_2$ + sensitizer + hν) does react with 1-arylalkenes, but the major reaction pathway involves a 2 + 4 cycloaddition leading to an endoperoxide rather than a 2 + 2 cycloaddition leading to a 1,2-dioxetane.[2,3] We have proposed that a benzo[*a*]pyrenyldioxetane is a minor but characteristic chemiluminescent intermediate formed during the microsomal metabolism of the carcinogenic benzo[*a*]pyrene-7,8-dihydrodiol (BP-diol).[4] We also have synthesized as BP-diol model compounds *cis*- and *trans*-1-(2′-methoxyvinyl)pyrene (*c*- and *t*-MVP, **1**) that cannot react with $^{1}O_2$ via an ene process.[5] MVP does react directly with $^{1}O_2$, but the 2 + 2 cycloaddition pathway leads (via the corresponding dioxetane **2**) to 1-pyrenecarboxaldehyde (**3**) in only 10% yield.[5] We report now that triphenyl phosphite ozonide [$(PhO)_3PO_3$, TPPO][6] and triethylsilyl hydrotrioxide ($Et_3SiOOOH$),[7] each prepared in situ from ozone, react at low temperature *directly* with MVP to produce pyrenyldioxetane **2** and then 1-pyrenecarboxaldehyde (**3**) on preparative scale in 20% and 34% yields, respectively (eq 1). These results demonstrate for the first time (1) *the superiority of TPPO and triethylsilyl hydrotrioxide over free $^{1}O_2$ for preparation of an aryldioxetane* and (2) *a direct reaction of triethylsilyl hydrotrioxide with an alkene.*



(1)

In methylene chloride solvent, TPPO at about −25 °C and triethylsilyl hydrotrioxide at about −60 °C release $^{1}O_2$.[6,7] Several diagnostic mechanistic experiments have been used to distinguish between oxygenation by free $^{1}O_2$ and oxygenation by direct, low-temperature reaction with TPPO. Schaap and Bartlett showed that, whereas $^{1}O_2$ reacted with *cis*- and with *trans*-1,2-diethoxyethylene stereospecifically (i.e., concerted 2 + 2 cycloaddition), TPPO reacted at −78 °C nonstereospecifically (i.e., via a stepwise mechanism involving direct reaction with TPPO);[8] in the absence of an electron-rich olefin, TPPO is stable at −78 °C and does not produce $^{1}O_2$.[6] Bartlett and Mendenhall showed that $^{1}O_2$ and TPPO at −78 °C have different selectivities toward tetramethylethylene and 2,5-dimethylfuran.[9] Sam and Sutherland reported that $^{1}O_2$ and TPPO at −70 °C gave different oxygenation products from the sesquiterpene germacrene.[10] Barlett and Chu demonstrated that the relative rates of 2 + 2 vs. ene oxygenation of dihydropyran were different using $^{1}O_2$ vs. TPPO at low temperature.[11] Stephenson and Zielinski used variously deuterated tetramethylethylenes to show via isotope effects that direct low-temperature TPPO–olefin reactions do not proceed through free $^{1}O_2$.[12]

Low-temperature (−60 °C) 400-MHz ^{1}H NMR analysis of a reaction between TPPO (1.1 equiv) and a mixture of *c*- and *t*-MVP in $CDCl_3$ revealed formation of pyrenyldioxetane **2** (δ 5.92 and 5.32, which peaks are characteristic of alkoxy- and aryldioxetanes)[1d] and an equal amount of another oxygenation product that may be the corresponding endoperoxide (δ 6.39 and 5.68; these "doublet" peaks coalesce to singlets at −2.5 °C and form "doublets" again upon cooling).[13] Upon warming the reaction mixture to room temperature, the characteristic dioxetane peaks at δ 5.92 and 5.32 disappeared, and a new aldehyde peak at δ 10.8 appeared, whereas the peaks at δ 6.39 and 5.68 remained. An internal NMR standard (mesitylene) indicated the pyrenyldioxetane **2** and ultimately the aldehyde **3** to be formed in 20% yield, along with 24% of unreacted MVP; no attempt was made to optimize consumption of MVP. Low-temperature ^{31}P NMR spectroscopy of the reaction between TPPO and MVP showed only one product signal characteristic of triphenyl phosphate.[8,11] Attempts to purify the reaction products chromatographically led, in all cases, to decomposition of the putative endoperoxide. Monitoring a low-temperature reaction between TPPO and MVP showed, upon warming to room temperature, a strong chemiluminescence (CL) characteristic of the excited state of 1-pyrenecarboxaldehyde.[4,5] Quantitative measurements of absolute photon yields indicated a significantly higher CL than that observed with free $^{1}O_2$; similar results were obtained using MVP and triethylsilyl hydrotrioxide.



(2)

Equation 2 is proposed as a reasonable working model for the mechanisms of these dioxygenation reactions. Nucleophilic attack by the electron-rich methoxyvinyl group of MVP on the central oxygen atom of TPPO and triethylsilyl hydrotrioxide produces oxonium intermediates as zwitterion **4a** in analogy to Schaap and Bartlett's proposal[8] (or the corresponding perepoxide)[14] and as ion pair **4b**,[15] respectively. Fragmentation of zwitterion **4a** and acid–base reaction of ion pair **4b** lead then to dioxetane **2**. An

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(1) For general review of 1,2-dioxetanes, see: (a) *Chemical and Biological Generation 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*, A. Hassner, Ed.; Wiley: New York, 1985; part 3, Chapter 4.

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(12) Stephenson, L. M.; Zielinski, M. B. *J. Am. Chem. Soc.* **1982**, *104*, 5819.

(13) The same NMR peaks were observed also starting with pure *cis*-MVP.

(14) cf.: Jefford, C. W.; Rimbault, C. G. *J. Am. Chem. Soc.* **1978**, *100*, 64379

(15) cf.: Curci, R.; Mello, R.; Troisi, L. *Tetrahedron* **1986**, *42*, 877.

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analogous mechanism involving radical[11] rather than ionic intermediates cannot be ruled out at this time.

1,1-Diphenyl-2-methoxyethylene reacted at low temperature also with TPPO and with triethylsilyl hydrotrioxide to produce benzophenone in 28% and 57% yields, respectively.[16,17] Even vinyl aromatics not activated by methoxyl substituents were converted by triethylsilyl hydrotrioxide into the corresponding 1,2-dioxetanes; TPPO did not react detectably (^1H NMR) with simple 1-arylalkenes at −60 °C even after 3 days. For example, 25–40 mg each of 1-vinylpyrene, 1-vinylnaphthalene,[18] and 2-vinylnaphthalene reacted with 1.8 equiv of triethylsilyl hydrotrioxide in methylene chloride (0.04 M),[7] slowly warmed during several hours from −78 → 25 °C and then kept at 25 °C for 12 h, to form the corresponding aromatic aldehydes (accompanied by CL during formation of 1-pyrenecarboxaldehyde) isolated by preparative TLC in 35%, 9%, and 23% yields (37%, 58%, and 59% yields based on recovered starting material), respectively. These results have both mechanistic and synthetic implications.

We are studying further the mechanism and the scope and limitations of these dioxetane-forming chemical reactions as well as biological applications.

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(16) (a) For $^1O_2$ reaction with 1,1-diphenyl-2-methoxyethylene, see: Steichen, D. S.; Foote, C. S. *Tetrahedron Lett.* **1979**, 4363. (b) For electron-transfer photooxygenation, see: Steichen, D. S.; Foote, C. S. *J. Am. Chem. Soc.* **1981**, *103*, 1855. (c) cf.: Matsumoto, M.; Kuroda, K. *Tetrahedron Lett.* **1979**, 1607. (d) For other enol ethers reacting with $^1O_2$, see: Asveld, E. W. H.; Kellogg, R. M. *J. Am. Chem. Soc.* **1980**, *102*, 3644.

(17) Ozonolysis of 1,1-diphenyl-2-methoxyethylene apparently leads to dimerization and rearrangement: Nakamura, N.; Nojima, M.; Kusabayashi, S. *J. Am. Chem. Soc.* **1986**, *108*, 4671 and references therein.

(18) For $^1O_2$ reaction with a vinyl aromatic proceeding apparently exclusively via an endoperoxide, see: (a) Matsumoto, M.; Kondo, K. *Tetrahedron Lett.* **1975**, 3935. (b) Matsumoto, M.; Dobashi, S.; Kondo, K. *Bull. Chem. Soc. Jpn.* **1977**, *51*, 185.

First Isolation of a Stable Aliphatic Thioaldehyde, Tris(trimethylsilyl)ethanethial

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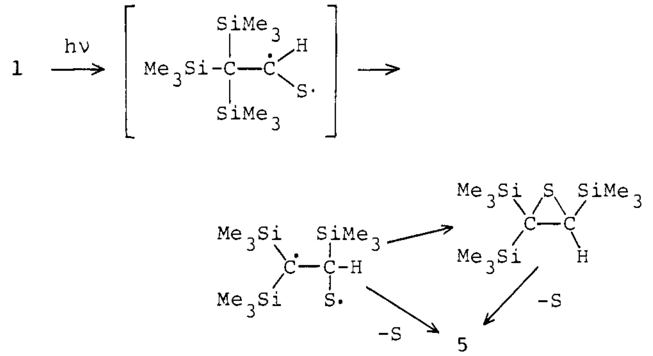
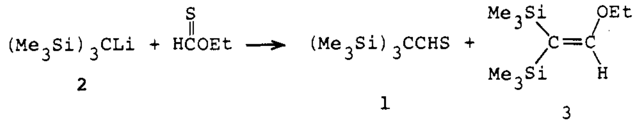
The chemistry of thioaldehydes has been of current interest.[1-9] Although many stable thioketones have been synthesized and relatively well studied in recent years, thioaldehydes have eluded isolation until very recently because of their extremely high tendency toward oligomerization.[10] We recently reported the first isolation of a stable aromatic thioaldehyde, 2,4,6-tri-*tert*-butylthiobenzaldehyde.[1] No aliphatic thioaldehyde, however, has been isolated so far although Vedejs and his co-workers have reported that thiopivaldehyde is relatively long-lived in solution (the half-life in chloroform at room temperature is 16 h).[2a,b] We now report the first isolation of a stable, crystalline, aliphatic thioaldehyde, tris(trimethylsilyl)ethanethial (**1**) and its interesting reactivities.

Scheme I



The reaction of tris(trimethylsilyl)methyllithium (**2**),[11] obtained from tris(trimethylsilyl)methane[12] and methyllithium, with *O*-ethyl thioformate gave the thioaldehyde **1** (16%)[13] and vinyl ether **3** (25%).[14,15]



2 1 3

Thioaldehyde **1** is a pink-red crystalline compound (mp 129–131 °C[16]) and can be purified by chromatography and recrystallization. It can be stored in a refrigerator for a long time without any decomposition and is stable at room temperature in the air at least for a week. Some spectral data of **1** are listed in Table I.

Although **1** is stable at room temperature, it undergoes Brook-type rearrangement[17] upon heating around 80 °C to give

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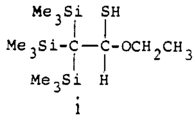
(13) A typical procedure of the synthesis of **1** follows. *O*-Ethyl thioformate (0.76 g, 8.5 mmol) was added to **2**, prepared from tris(trimethylsilyl)methane[12] (1.65 g, 7.08 mmol) and methyllithium (0.829 M solution of ether, 10.5 mL, 8.5 mmol) in THF (28 mL), at −78 °C. The pale yellow reaction solution was stirred for 10 min at −78 °C and for 1.5 h at room temperature. To the dark red solution were added aqueous ammonium chloride and ether. The dark red organic layer was separated, washed with brine 3 times, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. Residual dark red liquid was subjected to chromatography (silica gel, hexane–dichloromethane 20:1). The first fraction was 694 mg of a mixture of tris(trimethylsilyl)methane (19%) and **5** (25%). The second fraction was **1** (306 mg, 1.10 mmol, 16%), which was recrystallized from pentane (0.4 mL) at −78 °C to give pink-red crystals. Exact mass for $C_{11}H_{28}Si_3S$: 276.1219. Found: 276.1209. For spectra data, see Table I.

(14) The vinyl ether **3** is most probably produced by Peterson type reaction of i on silica gel.



i

(15) All new compounds gave satisfactory spectral data including exact mass analysis. For the details, see the supplementary material.

(16) Decolorization due to the isomerization into **3** began gradually at ca. 70 °C on measuring the melting point.

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