preparative reactions, the time for the reaction is best determined by GC analysis as reaction proceeds. In one experiment with 2-octyl methyl ether, 1 equiv of $HOTs \cdot H_2O$ was dissolved in the minimum volume of MeCN and added to the solution dropwise over 30 min, and reaction was >95% complete in 2 hr.

Influence of 2,4,6-Tri-*tert*-butylpyridine. When 2 or more equiv of 2,4,6-tri-*tert*-butylpyridine per equivalent of DCME are present in the initial solution, no cleavage of THF or cyclohexanone ketal was detected in 3 hr. If 1 equiv of the pyridine is used, THF yields ca. 50% cleavage products and cyclohexanone ketal is cleaved completely.

Cleavage of Ketals. Camphor and cyclohexanone ethylene glycol ketals were prepared by standard methods.[15] Cleavage was accomplished by the methods given above (Table I), but reaction time was always less than 5 min.

Carbon Monoxide Formation. DCME (10 mmol) and NaI (20 mmol) were dissolved in MeCN (20 ml of Spectrograde) and stirred at room temperature. Gas was evolved over 3 hr (134 ml, 6 mmol) and was collected in a gas buret. Mass spectroscopy and ir analysis identified the gas as CO. CO evolution was also detected during the ether cleavage reactions, but the quantities were smaller.

^{13}C Spectra of *exo*- and *endo*-Norbornyl Iodide. ^{13}C spectra were recorded on CFT-20 with proton noise decoupling on neat samples containing internal Me_4Si and acetone-d_6. Assignments were made on the basis of off-resonance proton-decoupled spectra.[16] Exo: 47.9, C-1; 45.1, C-3; 37.9, C-4; 36.2, C-7; 29.3, C-2; 28.6, 28.4, C-5 and C-6, not distinguished. Endo: 45.1, C-1; 43.7, C-3; 37.3, C-4; 36.3, C-7; 32.4, C-2; 29.9, 28.7, C-5 and C-6, not distinguished.

Acknowledgments. C.A.S. gratefully acknowledges the support of an NSF Graduate Fellowship. The Perkin-Elmer R-32 and Varian CFT-20 NMR spectrometers were purchased with NSF Departmental Grants 8370 and 7842, respectively. The support of a Frederick Gardner Cottrell grant from the Research Corporation is gratefully acknowledged.

Registry No.—Acetonitrile, 75-05-8; 1,1-diiododimethyl ether, 57132-06-6; hydriodic acid, 10034-85-2; dichlorodimethyl ether, 4885-02-3; (+)-(*S*)-2-octyl iodide, 1809-04-7; 2,4,6-tri-*tert*-butylpyridine, 20336-15-6; *endo*-norbornyl iodide, 57173-48-5; *exo*-norbornyl iodide, 30983-85-8.

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α-Hydroperoxy Acids via Direct Oxygenation[1]

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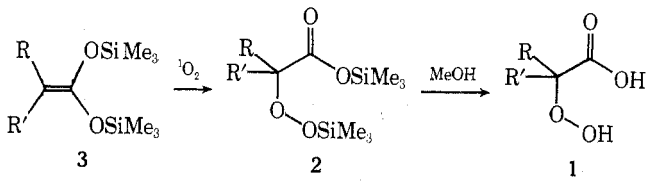
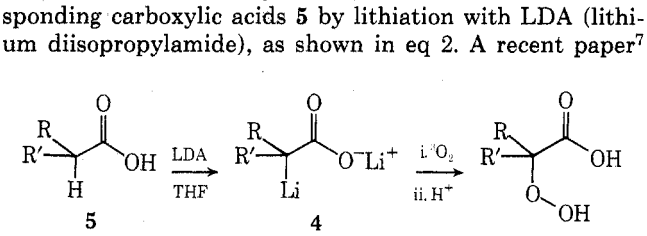
In the preparation of α-peroxylactones, which serve as active intermediates in bioluminescence,[2] we required the α-hydroperoxy acids **1** as precursors. We accomplished the preparation, isolation, and characterization of the first authentic α-hydroperoxy acids **1** by employing singlet oxygenation of the bis(trimethylsilyl) ketene acetals **3**, followed by desilylation of the bis(trimethylsilyl) derivative **2** with methanol (eq 1).[3] The success of our method rested on



(1)

the oxygenophilic nature of silicon, which promotes a silatropic shift with singlet oxygen, quite analogous to the classical ene reaction.[4] Simultaneously with oxygen fixation at the α carbon to the carbonyl group, the hydroperoxide and carboxylic acid functionalities are protected against base- and acid-catalyzed Grob fragmentation[5] of the hydroperoxy acid **1** by trimethylsilylation. The trimethylsilyl groups on one hand permit isolation and purification by distillation at reduced pressure, and on the other hand they permit quantitative release of the OOH and CO_2H functionalities by desilylation with neutral methanol.

The disadvantage of this novel oxygenation is that it lacks generality because secondary and primary alkyl groups in the ketene acetal **3** suffer prototropic shifts (ene reaction) with singlet oxygen. For this reason we investigated some time ago[6] the feasibility of the direct oxygenation of α-lithiocarboxylates **4**, derived from the corresponding carboxylic acids **5** by lithiation with LDA (lithium diisopropylamide), as shown in eq 2. A recent paper[7]



(2)

obliges us to communicate our results on this direct α-oxygenation of carboxylic acids **5** with triplet oxygen. Our experimental procedure is particularly advantageous for low molecular weight substrates which require special precautions in view of their thermal lability and high hygroscopic character. If the dianion **4** is prepared in the absence of HMPA, oxygenated at ca. −100 to −90° by slow addition of dianion **4** to an oxygen-saturated solution, protonated at −100°, and the work-up and purification carried out at subambient conditions, the degree of oxygenation can be effectively quantitative, affording crude α-hydroperoxide product in about 80%. Our recommended general procedure is described below and employed in the preparation of 2-hydroperoxy-2-methylpropionic acid (R = R′ = Me) and 3,3-dimethyl-2-hydroperoxybutyric acid (R = *t*-Bu; R′ = H).

Experimental Section

General Preparation of α-Hydroperoxy Acids. 1. α-Lithiation. A dry, 150-ml, two-necked, round-bottomed flask, provided with magnetic spinbar, rubber septum, and three-way stopcock, was attached to a nitrogen manifold and flushed with dry nitrogen for at least 5 min. While under a positive nitrogen pressure (ca. 50 mm, regulated with a mercury bubbler), the reaction vessel was charged by means of a syringe with 60 mmol of diisopropylamine (freshly distilled from calcium hydride) and 70 ml of anhydrous THF (freshly distilled from benzophenone ketyl radical). By means of a dry ice–methanol bath the reaction flask was cooled to −60 to −40° and while stirring vigorously, 63 mmol of *n*-butyllithium in *n*-hexane (standardized acidimetrically) was added with the help of a syringe. After complete addition (ca. 5 min), the cooling bath was removed and the reaction mixture allowed to reach room temperature (ca. 30°) while stirring. The reaction mixture was kept at room temperature for 10 min and cooled to −78° by means of a dry ice–methanol bath and a solution of 25 mmol of the carboxylic acid to be lithiated in 5 ml of anhydrous THF was added with the help of a syringe. Subsequently the reaction mixture was allowed to warm up to room temperature again and heated at 40° for 30 min while stirring. A pale yellow, clear solution of the dianion resulted, which exhibited a methyl iodide assay of better than 98% lithiation by NMR.

2. α-Oxygenation. A dry 250-ml, three-necked, round-bottomed flask, supplied with an efficient, hermetically sealed mechanical stirrer, a rubber septum, and a three-way stopcock, was attached to the nitrogen manifold and flushed with dry nitrogen. The flask was charged with 70 ml of anhydrous THF with the help of a syringe and cooled to −100 to −90° by means of a liquid nitrogen–THF bath, while keeping a positive nitrogen pressure (ca. 50 mm). The THF solution was saturated efficiently (ca. 10 min) with dry oxygen gas, allowed to enter through the rubber septum by means of a syringe needle. With the help of stainless steel capillary tubing (12G) as syphon, the dianion solution was transferred dropwise over a period of 1–2 hr (the dropping rate regulated with a blood serum proportionator which was attached to a nitrogen balloon) into the oxygen-saturated THF solution, keeping the oxygenation vessel at −100 to −90°, while passing a vigorous stream of dry oxygen gas through the reaction mixture during the entire process.

3. Hydrolysis. After complete addition of the dianion solution (ca. 1–2 hr), under efficient mechanical stirring and keeping the reaction mixture at −100 to −90°, by means of a syringe 120–125 mmol of a 15% aqueous hydrochloric acid solution was added. The resulting "sherbetlike" mixture was allowed to warm up to ca. −20° and transferred into a 500-ml separatory funnel, which contained 80 ml of NaCl-saturated ice water. The aqueous layer was efficiently extracted with ether (ca. 5 × 25 ml) and methylene chloride (ca. 3 × 25 ml), keeping the temperature during the extraction process between 0 and 5° by adding ice and NaCl. The combined organic extracts were dried over anhydrous $MgSO_4$ at 0°. The solvent was removed by rotary evaporation [−5 to 0° (3–4 mm)]. The oxygenation product was obtained as a colorless oil (ca. 95–100% crude yield), which crystallized on standing in the freezer. Iodometric analysis indicated a ca. 80% peroxide titer based on α-hydroperoxy acid. The crude product must be purified without delay at subzero temperature to minimize decomposition.

Preparation of 2-Hydroperoxy-2-methylpropionic Acid. Following the general procedure, 25 mmol of 2-methylpropionic acid was converted in 97% crude yield to the corresponding α-hydroperoxy acid, exhibiting a 81% peroxide titer by iodometry. In view of its low thermal stability in the impure state (above 10° it decomposes with gas evolution) and high hygroscopic nature (dry crystals allowed to come in contact with atmospheric moisture diffuse within seconds), the crude product was recrystallized immediately several times from ether–pentane mixture at 5° in a glove bag under a dry nitrogen atmosphere. The crystalline product was obtained as white needles, better than 97% pure by iodometry, mp 44–46°, with gas evolution at 74°. The spectral data follow: 60-MHz NMR (CCl_4) δ (Me_4Si) 9.7 (2 H, singlet, $-CO_2H$ and $-O_2H$) and 1.5 ppm (6 H, singlet, $-CH_3$); ir (CCl_4) 3660 and 3480 (–OOH and $-CO_2H$), 3000–2800 (aliphatic CH), 1710 (carbonyl), and 1380 and 1360 cm^{-1} (*gem*-dimethyl).

Preparation of 3,3-Dimethyl-2-hydroperoxybutyric Acid. Following the general procedure, 25 mmol of 3,3-dimethylbutyric acid was converted in 93% crude yield to its corresponding α-hydroperoxy acid, exhibiting 78% peroxide titer by iodometry. The crude product was purified immediately by repeated recrystallization from ether–hexane mixture, preventing exposure to atmospheric moisture. Colorless needles were obtained, better than 99% pure by iodometry, mp 68–70° (lit.[3] 69–70°), with gas evolution at 74°. The spectral data follow: 60-MHz NMR (CCl_4) δ (Me_4Si) 10.3 (2 H, singlet, $-CO_2H$ and $-O_2H$), 4.3 (1 H, singlet, CH), and 1.0 ppm (9 H, singlet, *tert*-butyl); ir (CCl_4) 3500–3000 ($-CO_2H$ and $-O_2H$), 2960 (aliphatic CH), 1715 (carbonyl), and 1370 cm^{-1} (*tert*-butyl).

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Registry No.—1 (R = R′ = Me), 57196-76-6; 1 (R = H; R′ = *t*-Bu), 36156-92-0; **5** (R = R′ = Me), 79-31-2; **5** (R = H; R′ = *t*-Bu), 1070-83-3.

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Studies Directed toward a Practical Synthesis of Brevicomin. IV. Formation and Hydrogenolysis of 5,7-Dimethyl-6,8-dioxabicyclo[3.2.1]octane under Catalytic Hydrogenation Conditions

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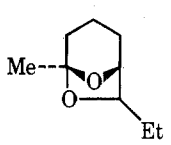
During the course of our investigations toward a practical synthesis of brevicomin (1), the aggregating sex pheromone of the pine bark beetle (*Dendroctonus brevicomis*),[1] we had the occasion to examine the hydrogenation of **2** → **3**. To our surprise we found a 13% yield of **4** as a secondary product of the reaction.[1c] In this paper we will present our findings on some of the unique chemistry associated with the reactions.



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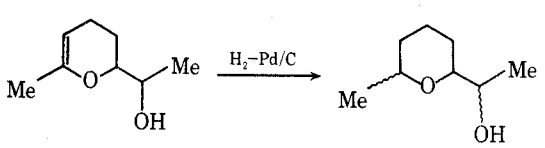

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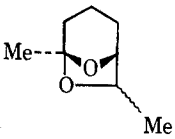

4

Attempts at utilizing this as a methodology for preparing, in high yield, bicyclic ketals of the type **4** met with uniform failure. Since we could not obtain increased yields of **4** we next decided to analyze whether or not **4** might simply be an intermediate in the reduction of **2** → **3**.