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SYNTHESIS OF α,ω-DICARBOXYLIC ACIDS AND UNSATURATED CARBOXYLIC ACIDS FROM SILYL ENOL ETHERS

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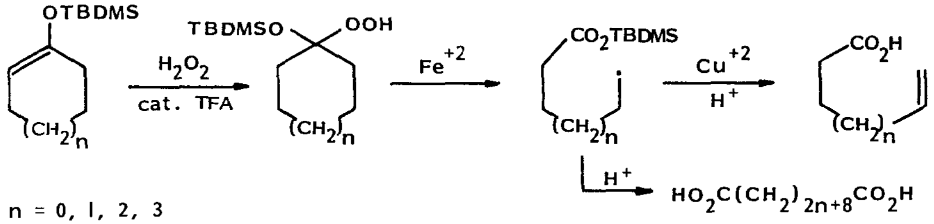
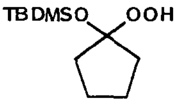
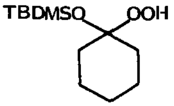
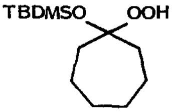
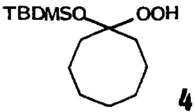
Summary: *The synthesis of α,ω-dicarboxylic acids and unsaturated monocarboxylic acids by metal-ion promoted ring-opening of cyclic α-t-butyldimethylsilyloxy hydroperoxides has been described.*

Metal-ion promoted ring-opening of cycloalkyl hydroperoxides has long been known as a synthetically useful reaction since its discovery in the early 1950s.[1] Since the traditional method usually employs mixture of peroxides obtained from the reaction of cyclic ketones with hydrogen peroxide in the presence of strong acids because of the incapability to isolate unstable 1-hydroxycycloalkyl hydroperoxides, undesirable by-product formation and a separation from staring ketones are inevitable.[1,2] In addition, this method is only effective for relatively reactive cyclic ketones such as cyclopentanone and cyclohexanone and cannot be applied to larger-membered cyclic ketones or cyclic enones. We previously reported an effective method for the synthesis of α-silyloxy hydroperoxides from a wide range of ketones, including cyclic enones, by converting them to *t*-butyldimethylsilyl enol ethers followed by acid-catalyzed addition with hydrogen peroxide.[3] We now wish to report a general, efficient method for converting silyl enol ethers to α,ω-dicarboxylic acids having double the number of carbon atoms originally present in the ketones and to monocarboxylic acids possessing terminal methylene groups by a route outlined below.

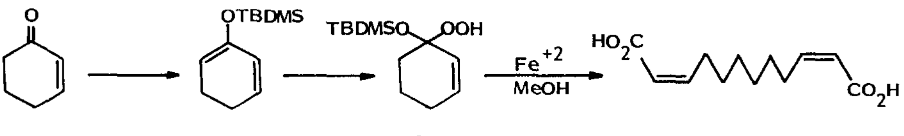


t-Butyldimethylsilyl (TBDMS) enol ethers are readily available from the corresponding ketones (LDA/TBDMSCl/THF-HMPA). α-*t*-Butyldimethylsilyloxy hydroperoxides (**1**∼**4**, **6**, **8**) were prepared in good yields by the reaction of the corresponding silyl enol ethers with hydrogen peroxide in the presence of a catalytic amount of trifluoroacetic acid (TFA) as described previously.[3] Addition of α-silyloxy hydroperoxide **1** to a solution of $FeSO_4$ (1.2 equiv mol) in methanol at 0 °C under nitrogen and successive acid hydrolysis of the resulting silyl esters gave after usual workup 1,12-dodecanedioic acid (54%). Other examples are shown in Table I. Notably, the reaction of α-silyloxy hydroperoxide **6** obtained from O-silylated

TABLE I[a]

ENTRY	HYDROPEROXIDE	PRODUCT	YIELD (%)[b]
1	 **1**	$HO_2C(CH_2)_8CO_2H$	54
2	 **2**	$HO_2C(CH_2)_{10}CO_2H$	53
3	 **3**	$HO_2C(CH_2)_{12}CO_2H$	68
4	 **4**	$HO_2C(CH_2)_{14}CO_2H$	72

[a] The reaction was conducted in methanol using $FeSO_4$ (1.2 equiv mol) at 0 °C under nitrogen. After the reaction the mixture was treated with 1 N H_2SO_4 at room temperature.
[b] Isolated yield.

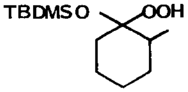


5 **6** (76%) **7** (87%)

1,3-cyclohexadien-2-ol 5 produced (2Z, 10Z)-2,10-dodecadien-1,12-dioic acid[4] (7, 87%) in a regiospecific fashion, with no isomeric olefins being detected.

It has been well recognized that the carbon radical intermediates produced by metal-ion induced decomposition of hydroperoxides is oxidatively intercepted by cupric salts to result in the formation of products of substitution and elimination.[5] When a methanolic solution of $FeSO_4$ (1.2 equiv mol) was added dropwise to a solution of α-silyloxy hydroperoxide and $Cu(OAc)_2$ (3.6 equiv mol) in methanol at 0 °C under nitrogen, unsaturated monocarboxylic acid was obtained in moderate yield. Table II details the results.[6] We already observed a stereospecific formation of (2Z)-2,5-hexadienoic acid from 6,[3] whereas the $Cu(OAc)_2$-$FeSO_4$ promoted fragmentation of 8 gave a 1:1 mixture of 9 and 10 in 77% yield.

TABLE II[a]

ENTRY	HYDROPEROXIDE	PRODUCT	YIELD (%)[b]
1	**2**		53
2	**3**		44
3	**4**		73
4	 **8**	 **9**  **10**	77

[a] The reaction was conducted in methanol using $FeSO_4$ (1.2 equiv mol) and $Cu(OAc)_2$ (3.6 equiv mol) at 0 °C under nitrogen. After treatment with 1 N H_2SO_4, the mixture was extracted with ether and purified by silica gel column chromatography. [b] Isolated yield after column chromatography.

The simple substrates chosen in this study may illustrate the utility of α-silyloxy hydroperoxides in the synthesis of dicarboxylic acids and unsaturated carboxylic acids. The easy availability of reasonably stable α-silyloxy hydroperoxides combined with their high solubility in usual organic solvents suggests a more significant role for the metal-ion promoted reactions of α-silyloxy hydroperoxides in organic synthesis.[7]

REFERENCES AND NOTES

(1) For a review, see (a) G. Sosnovsky and D. J. Rawlinson "Organic Peroxides", D. Swern, ed., Wiley-Interscience, New York, 1971, Vol. II. Chapter II. (b) F. Minisci, Synthesis, 1 (1973).

(2) For example, see E. G. E. Hawkins, *J. Chem. Soc.*, **1955**, 3463.

(3) I. Saito, R. Nagata, K. Yuba and T. Matsuura, *Tetrahedron Lett.*, **24**, 1737 (1983).

(4) Mp 120-122 °C; ^{1}H NMR (CD_3COCD_3) δ 1.00-1.90 (m, 8 H), 2.40-2.90 (m, 4 H), 5.70 (d, 2 H, J = 12.5 Hz), 6.30 (dt , 2 H, J = 12.5, 6 Hz), 9.50 (br s, 2 H).

(5) (a) J. K. Kochi, "Free Radicals", Wiley-Interscience, New York, 1973, Vol. 1, Chapter 11, Vol. 2, Chapter 23. (b) B. Acott and A. L. J. Beckwith, *Aust. J. Chem.*, **17**, 1342 (1964). (c) For a recent synthetic application, see S. L. Schreiber, *J. Am. Chem. Soc.*, **102**, 6163 (1980).

(6) The following procedure is representative. To an ice-cooled solution of $Cu(OAc)_2$ (1.30 g, 7.2 mmol) in methanol (40 mL) was added α-silyloxy hydroperoxide **4** (548 mg, 2 mmol) by syringe under stirring. A solution of $FeSO_4\cdot7H_2O$ (667 mg, 2.4 mmol) in methanol (10 mL) was added dropwise to this solution. The resulting mixture was stirred for 30 min under nitrogen, then treated with 1 N H_2SO_4 (10 mL) for 1 h and extracted with ether. The extracts were dried over anhydrous Na_2SO_4 and evaporated. The residue was chromatographed on a silica gel column to give 7-octenoic acid (207 mg, 73%).

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