directly by thionyl chloride, the following experiment was performed. The starting acid (5.3 g, 0.025 mol) was treated with $SOCl_2$ (10 ml) at 110°. After 1.5 hr the NMR spectrum of the reaction mixture showed that the α proton was not replaced. Therefore **12a** could not be obtained in the absence of iodine. At a higher temperature (130°) and upon a longer period of heating (overnight) there was ca. 40% α-chlorination.

(30) W. M. Weaver and J. D. Hutchison, *J. Am. Chem. Soc.*, **86**, 261 (1964).
(31) The lack of displacement of I^- by Cl^- might be due to the fact that HCl in the experimental conditions was not sufficiently dissociated.
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(33) (a) R. N. McDonald and R. A. Krueger, *J. Org. Chem.*, **28**, 2542 (1963); (b) A. J. Krubsack and T. Higa, *Tetrahedron Lett.*, 4515 (1973).
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Hydroxylation of Carbonyl Compounds via Silyl Enol Ethers[1a]

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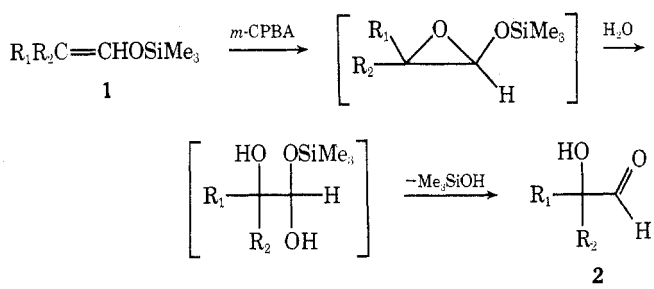
Silyl enol ethers **1**, which are readily available from the corresponding aldehydes, react rapidly with *m*-chloroperbenzoic acid to afford the protected α-hydroxy aldehydes **3** in good yield. Treatment of **3** with acetic anhydride and triethylamine produces α-acetoxy aldehydes **5**. This sequence provides a simple procedure for α-hydroxylation of aldehydes. Silyl enol ethers of ketones **10** are converted directly to α-siloxy ketones **11** with *m*-chloroperbenzoic acid representing a significant improvement over the usual enol ether or acetate procedure.

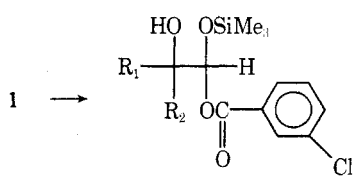
The effectiveness of trimsyl[1d] enol ethers **1** as masked aldehydes, ketones, and even acids or esters in reactions with electrophiles such as halogens or NOCl has recently been demonstrated.[2] We have now examined the reaction of **1** with peracids, as a potential route to siloxy epoxides or to α-hydroxy carbonyl compounds[3] which are of current interest in sugar synthesis and as precursors to β-hydroxy-α-amino acids.[4] Until recently there were no satisfactory methods available for the synthesis of α-hydroxy aldehydes.[5a] Several procedures have now been described, but they represent homologation reactions.[4,5]

A simple operation was envisioned which would proceed via the epoxidation of trimsyl enol ethers **1** with *m*-chloroperbenzoic acid (*m*-CPBA) followed by hydrolysis and β-cleavage of trimsyl alcohol[6] to afford the desired product **2** as shown in Scheme I. However, the observed product was

Scheme I



not the hydroxy aldehyde **2**, but the acetal derivative **3**, which is probably generated by opening of the intermediate epoxide by *m*-chlorobenzoic acid or by trapping of an intermediate cation by this acid. The in situ ring opening of α-

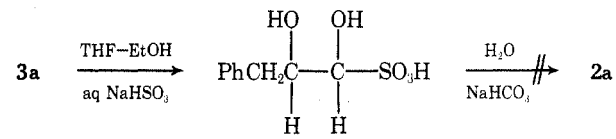


alkoxy epoxides, derived from vinyl ethers, by carboxylic acids is a well-known reaction.[7] Attempts to trap the epoxide as the aldehyde by reaction in aqueous THF and as the dimethyl acetal by reaction in methanol afforded uncharacterized mixtures. Hydrogen peroxide (30%) in THF produced only the parent aldehyde via hydrolysis.

Equimolar amounts of **1** and *m*-chloroperbenzoic acid reacted rapidly at room temperature in dichloromethane. After 1 hr, work-up yielded **3** in high yield (Table I). The structure of the product was confirmed by ir, NMR, and mass spectral data. The technique is applicable to a wide range of aldehydes. Thus, R may be alkyl, aryl, or hydrogen. Particularly noteworthy is the presence of a double bond (entry **1f**) and an ester function (**1c**).

It is well known that α-hydroxy aldehydes **2** are quite unstable and rapidly rearrange to hydroxy ketones, dimerize, and polymerize.[5] Generally, compounds **2** are generated in a protected form such as an acetal and converted to the parent **2** only with difficulty.[5] Similar difficulties were encountered in this work. Thus, when **3a** was treated with fluoride ion in Me_2SO or THF,[7] hydrochloric acid in methanol, or aqueous sodium hydroxide in THF, the desired aldehyde **2a** was not obtained. Pyrolysis of **3a** also failed to produce **2a** by expulsion of trimsyl *m*-chlorobenzoate. Finally, an effort to convert **3a** to the siloxy derivative of **2a** by generation of the alkoxide ion by LiH followed by intramolecular silicon transfer also failed. No effort was made to determine the course of these reactions once it was found that the desired transformation was not occurring.

An uncharacterized red oil was obtained from phenylhydrazine and **3e** rather than the desire osazone.[9a] Treatment of **3a** with a standard solution of sodium bisulfite afforded sulfonate **4**.[9b] However, when **4** was stirred with aqueous



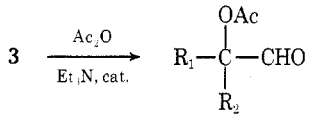
sodium bicarbonate, **2a** was not obtained, but instead an uncharacterized mixture which appeared to contain mostly the dimer of **2a** was recovered. Attempted protection of the hydroxyl function of **3** as an *O*-methyl ether by reaction with methyl Meerwein reagent or methyl iodide and silver oxide or sodium hydride resulted in polymeric products.

Successful deblocking of **3** to generate acetoxy aldehyde

Table I
Synthesis of Protected α-Hydroxy Aldehydes 3 from Silyl Enol Ethers 1

Entry	R_1	R_2	% yield of 3
1a	Ph	Me	85
1b	$PhCH_2$	H	72
1c	$-CH_2CH_2CH_2CH(CO_2Et)CH_2-$		93
1d	Me	Me	74
1e	C_8H_{17}	H	84
1f	$-CH_2CH_2CH{=}CHCH_2-$		79

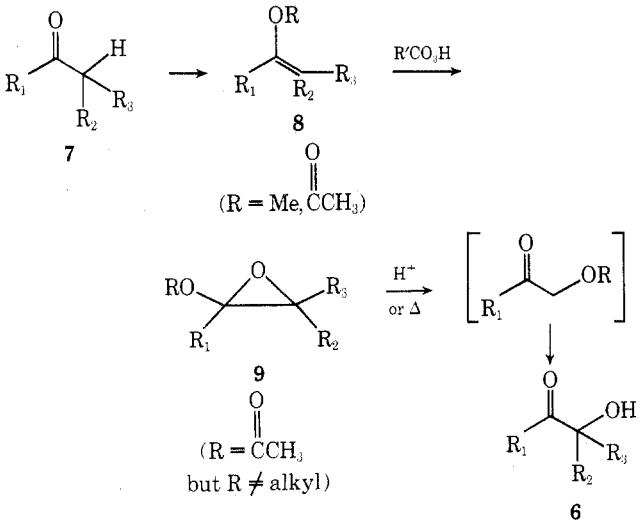
5 was achieved by reaction with excess acetic anhydride and triethylamine in the presence of a catalytic amount of 4-pyrrolidinopyridine.[10] Presumably, this represents an acylation followed by deblocking of the aldehyde. The percent conversion of 1 to 5 is only modest but related synthetic procedures for conversion of aldehydes to their α-hydroxy derivatives do not appear to be available.[11] Table II shows the results of the direct conversion of silyl enol ether 1 to acetoxy aldehyde 5 without isolation of the intermediate 3.



5

There are several synthetic procedures available for α-hydroxy ketones. The acyloin reaction[12] is the best known, but there are several other homologation reactions.[13] Some ketones with an α carbon bearing only one hydrogen can be converted to the corresponding α-hydroxy derivative upon treatment with base and oxygen followed by reduction of the intermediate hydroperoxide with zinc or trialkyl phosphites.[14] With most ketones this procedure results in α diketones and α-cleavage products.

A convenient procedure for regiospecific synthesis of α-hydroxy ketones 6 from the parent ketones 7 is the reaction of enol ether or acetate derivatives 8 of the ketone with peracids.[14] The intermediate epoxides 9 can be converted to the desired 6 by acid or heat followed by hydrolysis.



Since regioselective formation of 8 can readily be achieved, the procedure represents a regioselective synthesis of the desired hydroxy ketone 6. A further convenient hydroxylation of enolates using MoO_5 has recently been reported.[15]

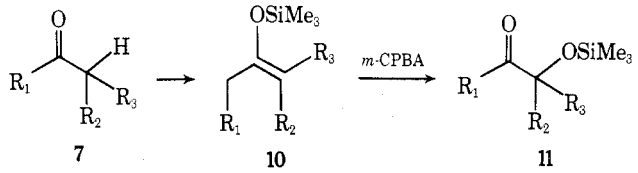
We have observed that extention of the peroxidation procedure to silyl enol ethers of ketones 10[3] allows the hydroxylation of 7 to 6 to be carried out much more conveniently, since the α-siloxy ketones 11 are obtained directly (Table III).[16] Furthermore, the transformation of ketones to 10 can be accomplished regiospecifically in high yields,[17] and silyl ethers are more readily hydrolyzed to alcohols than acetates or ethers.

Table II
Synthesis of α-Acetoxy Aldehydes 5 from Silyl Enol Ethers 1

Entry	R_1	R_2	% yield of 5
1b	$PhCH_2$	H	42
1c	$-CH_2CH_2CH_2CH(CO_2Et)CH_2-$		45
1e	C_8H_{17}	H	46
1f	$-CH_2CH_2CH{=}CHCH_2-$		39

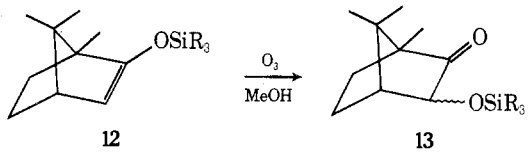
Table III
Synthesis of α-Siloxy Ketones 11 from Silyl Enol Ethers 10

Entry	R_1	R_2	R_3	% yield of 11
10a	Ph	Me	H	90
10b	Et	Me	H	75
10c	t-Bu	H	H	73



7 10 11

A related reaction has been observed by Heathcock.[18] Treatment of silyl enol ethers with ozone generally results in cleavage of the olefinic double bond as expected. However, when 12 was treated with ozone rearrangement occurred to afford α-siloxy ketone 13. Similar transformations were also reported for ketene silyl acetals.



12 13

Experimental Section[19]

Preparation of Silyl Enol Ethers. The procedure by House[17a] employing trimsyl chloride and triethylamine in DMF was used to afford products in 60–80% yield.

Epoxidation of Silyl Enol Ethers 1. To a stirred solution of 1 in dichloromethane was added portionwise over several minutes 1.1 equiv of 85% *m*-chloroperbenzoic acid (Aldrich). In the synthesis of some α-siloxy ketones the addition of solid $NaHCO_3$ avoids hydrolysis of the silyl group. After the resulting solution was stirred for 1 hr, aqueous Na_2SO_3 was added to destroy excess peroxide. The solution was washed with aqueous $NaHCO_3$, and the organic layer was dried and concentrated in vacuo. The hydroxy aldehyde derivatives 3 are difficult to purify and were converted to 5 as described below, while the siloxy ketones 11 were purified by bulb-to-bulb distillation. Though these compounds are difficult to obtain analytically pure, elemental analysis was performed on representative samples (5e and 11a) and NMR and mass spectral data as well as analogous reports on α-hydroxy ketones[3] are consistent with the assigned structures.

1-Trimethylsiloxy-1-*m*-chlorobenzoxy-2-phenyl-2-propanol (3a). From 1.03 g (5 mmol) of 1a was obtained 1.60 g (85%) of colorless, viscous oil 3a as a 7:3 erythro/threo mixture: ir (neat) 3500 (OH), 1720 cm^{-1} (ester); NMR ($CDCl_3$) δ 0.1 (s, 9, $SiMe_3$), 1.8 (s, 3, Me), 3.3 (s, 1, OH), 6.3 (s, 1, CH), 7.5 (m, 7, aromatic), 8.0 (m, 2, aromatic); 0.3 (s, 9, $SiMe_3$), 1.6 (s, 3, Me), 3.3 (s, 1, OH), 6.4 (s, 1, CH), 7.5 (m, 7, aromatic), 8.0 (m, 2, aromatic).

1-Trimethylsiloxy-1-*m*-chlorobenzoxy-3-phenyl-2-propanol (3b). From 1.03 g (5 mmol) of **1b** was obtained 1.35 g (72%) of colorless, viscous oil **3b:** NMR ($CDCl_3$) δ 0.1 (s, 9, $SiMe_3$), 2.3 (s, 1, OH), 2.8 (m, 2, CH_2), 3.8 (m, 1, CH), 6.10 (d, 1, CH), 7.2 (s, 5, Ph), 7.4 (m, 2, Ph), 7.9 (m, 2, Ph).

Ethyl [3-Hydroxy-3-(trimethylsiloxy-*m*-chlorobenzoxy)-methyl]cyclohexanecarboxylate (3c). From 1.38 g (5 mmol) of **1c** was obtained 2.0 g (93%) of colorless, viscous oil **3c:** NMR ($CDCl_3$) δ 0.1 (s, 9, $SiMe_3$), 1.2 (t, 3, CH_3), 1.5 (m, 9, ring protons), 2.5 (s, 1, OH), 4.1 (q, 2, CH_2), 5.9 (s, 1, CH), 7.5 (m, 2, aromatic), 8.0 (m, 2, aromatic).

1-Trimethylsiloxy-1-*m*-chlorobenzoxy-2-methyl-2-propanol (3d). From 0.72 g (5 mmol) of **1d** was obtained 1.17 g (74%) of colorless, viscous oil **3d:** NMR ($CDCl_3$) δ 0.1 (s, 9, $SiMe_3$), 1.2 (s, 6, Me_2C), 2.5 (s, 1, OH), 5.9 (s, 1, CH), 7.4 (m, 2, aromatic), 8.4 (m, 2, aromatic).

1-Trimethylsiloxy-1-*m*-chlorobenzoxy-2-decanol (3e). From 1.14 g (5 mmol) of **1e** was obtained 1.68 g (84%) of viscous, colorless oil **3c:** NMR ($CDCl_3$) δ 0.1 (s, 9, $SiMe_3$), 0.9 (m, 3, Me), 1.2 [m, 14, $(CH_2)_7$], 2.8 (s, 1, OH), 3.6 (m, 1, CH), 6.0 (d, 1, CH), 7.4 (m, 2, aromatic), 7.9 (m, 2, aromatic).

4-Hydroxy-4-(trimethylsiloxy-*m*-chlorobenzoxy)methylcyclohexene (3f). From 0.91 g (5 mmol) of **1f** was obtained 1.40 g (79%) of viscous, colorless oil **3f:** NMR ($CDCl_3$) δ 0.1 (s, 9, $SiMe_3$), 1.5–2.5 (broad, 6, ring protons), 2.4 (s, 1, OH), 5.6 (m, 2, -CH=CH-), 5.9 (s, 1, CH), 7.4 (m, 2, aromatic), 7.9 (m, 2, aromatic).

Synthesis of α-Acetoxy Aldehydes 5. The crude products **3** from above were dissolved in dry ether and 1 ml of acetic anhydride, 2 ml of triethylamine, and 0.02 g of 4-pyrrolidinopyridine[10] were added. After stirring for 15 min methanol was added to destroy excess acetic anhydride. The solution was washed with aqueous saturated sodium bicarbonate, 1.5 *M* aqueous hydrochloric acid, and water. The ether was dried (K_2CO_3) and concentrated in vacuo to afford crude **5,** which was purified by bulb-to-bulb distillation.

2-Acetoxy-3-phenylpropanol (5b). From 1.03 g (5 mmol) of **1b** was obtained 0.45 g (42%) of colorless oil **5b:** bp 110° (0.1 Torr); ir (neat) 1730 cm^{-1} (C=O); NMR ($CDCl_3$) δ 2.0 (s, 3, CH_3), 2.9 (d of d, 2, CH_2), 5.2 (d of d, 1, CH), 7.3 (s, 5, Ph), 9.5 (s, 1, CHO).

Ethyl 3-Acetoxy-3-formylcyclohexanecarboxylate (5c). From 1.38 g (5 mmol) of **1c** was obtained 0.55 g (45%) of colorless oil **5c:** bp 100° (0.1 Torr); NMR ($CDCl_3$) δ 1.2 (t, 3, CH_3), 1.0–3.0 (m, 9, ring protons), 2.2 (s, 3, CH_3), 4.1 (q, 2, CH_2), 9.4 (s, 1, CHO).

2-Acetoxydecanal (5e). From 1.14 g (5 mmol) of **1e** was obtained 0.55 g (51%) of colorless oil **5e:** bp 100° (0.1 Torr); NMR ($CDCl_3$) δ 0.9 (t, 3, CH_3), 1.0–2.0 [br, 14, $(CH_2)_2$], 2.1 (s, 3, CH_3), 4.9 (t, 1, CH), 9.4 (s, 1, CHO). Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.18; H, 10.35.

4-Acetoxy-4-formylcyclohexene (5f). From 0.91 g of **1f** was obtained 0.33 g (39%) of colorless oil **5f:** bp 90° (0.1 Torr); NMR ($CDCl_3$) δ 1.4–2.8 (m, 6, ring protons), 2.1 (s, 3, CH_3), 5.65 (s, 2, -CH=CH-), 9.5 (s, 1, CHO).

α-Trimethylsiloxypropiophenone (11a). From 1.03 g (5 mmol) of **10a** was obtained 0.96 g (90%) of colorless oil **11a:** bp 85° (0.6 Torr); NMR ($CDCl_3$) δ 0.1 (s, 9, $SiMe_3$), 1.4 (d, 3, CH_3), 5.0 (q, 1, CH), 7.4 (M, 3, aromatic), 8.0 (m, 2, aromatic). Anal. Calcd for $C_{12}H_{18}O_2Si$: C, 64.82; H, 8.16. Found: C, 64.92; H, 8.15. Calcd for $C_{12}O_{18}O_2Si$: M^+ 222.107. Found: 222.085.

2-Trimethylsiloxy-3-pentanone (11b). From 0.80 g (5 mmol) of **10b** was obtained 0.65 g (75%) of colorless **11b:** bp 80° (8 Torr); NMR ($CDCl_3$) δ 0.1 (s, 9, $SiMe_3$), 1.0 (t, 3, CH_3), 1.2 (d, 3, CH_3), 2.5 (q, 2, CH_2), 4.05 (q, 2, CH).

1-Trimethylsiloxy-3,3-dimethyl-2-butanone (11c). From 0.86 g (5 mmol) of **10c** was obtained 0.69 g (73%) of colorless oil **11c:** bp 70° (10 Torr); NMR ($CDCl_3$) δ 0.1 (s, 9, $SiMe_3$), 1.15 (s, 9, *t*-Bu), 4.35 (s, 2, CH_2).

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Registry No.—**1a,** 51075-23-1; **1b,** 51075-22-0; **1c,** 55638-14-7; **1d,** 6651-34-9; **1e,** 51075-24-2; **1f,** 51075-25-3; *erythro*-**3a,** 55638-15-8; *threo*-**3a,** 55638-16-9; **3b,** 55638-17-0; **3c,** 55638-18-1; **3d,** 55638-19-2; **3e,** 55638-20-5; **3f,** 55368-21-6; **5b,** 38559-23-8; **5c,** 55638-22-7; **5e,** 55638-23-8; **5f,** 55638-24-9; **10a,** 37471-46-8; **10b,** 17510-47-3; **10c,** 17510-46-2; **11a,** 55638-25-0; **11b,** 55638-26-1; **11c,** 55638-27-2; *m*-chloroperbenzoic acid, 937-14-4; acetic anhydride, 108-24-7.

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