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Regioselective Synthesis of Δ^3-Butenolides via Oxidation of 2-Trimethylsilylfurans

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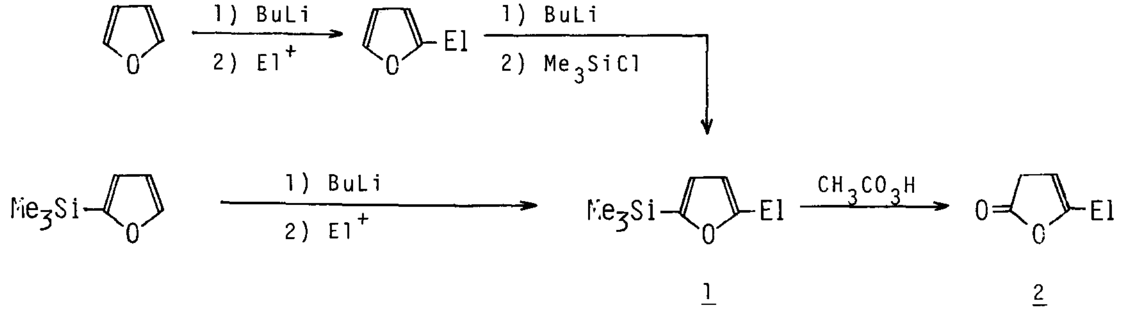
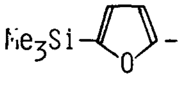
Summary: 5-Alkyl-2-trimethylsilylfurans, easily accessible via successive alkylation and silylation of furan, undergo oxidation cleanly with peracetic acid to afford the corresponding Δ^3-butenolides in good yields.

Among enol lactones, Δ^3-butenolides1) are most widely employed as useful synthetic units for carbon-carbon bond formation and introduction of functional groups.2) A common method for their synthesis involves intramolecular dehydration of the corresponding γ-keto acids. However, reaction conditions employed in the above procedure, e.g. heating in acetic anhydride, are sometimes too vigorous for other functional groups to survive, and often bring about concomitant formation of isomeric Δ^2-butenolides. 2-Substituted furans have also been used as precursors for butenolides, but their oxidation usually gives isomeric Δ^2-butenolides, accompanying migration of the double bond.3)

We have found that 2-trimethylsilylfurans are cleanly oxidized to the Δ^3-butenolides 2 on treating with peracetic acid as depicted in Eq 1. Starting



(Eq. 1)



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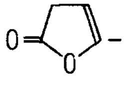

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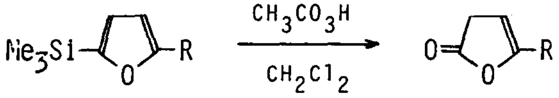
materials 1 are easily accessible via successive alkylation followed by silylation of furan, or more conveniently by alkylation of 2-trimethylsilylfuran.[4)] The above equation indicates that in the present method 2-trimethylsilylfuran works as an anionic equivalent 4 and various electrophiles can be introduced onto the 4-position of the butenolide.

The results of their oxidation are listed in the Table. As an oxidant, peracetic acid (4 eq) gave satisfactory results. Use of m-CPBA reduced the product yield remarkably. This may be attributable to its higher oxidizing ability to result in a lack of regioselectivity. t-Butyl hydroperoxide with titanium isopropoxide[5)] was ineffective for this oxidation. Although there

Table. Oxidation of 2-Trimethylsilylfurans.[a]



Run	R	Yield[b] (%)
1	C_6H_{13}-	84
2	$(CH_3)_2CHCH_2CH_2$-	78
3	$CH_2{=}CH(CH_2)_9$-	65
4	$(EtO)_2CHCH_2CH_2$-	73
5	$C_8H_{17}CH(OH)$-	<30[c]
6	$C_8H_{17}CH(O\underset{\text{t-Bu}}{\underset{\mid}{\text{Si}}}Me_2)$-	64[d]
7	$C_8H_{17}CH(OAc)$-	trace
8	$C_8H_{17}CH(OH)CH_2$-	36[c]
9	$C_8H_{17}CH(O\underset{\text{t-Bu}}{\underset{\mid}{\text{Si}}}Me_2)CH_2$-	73[e]
10	C_4H_9O-CO-	No Reaction[f]

[a] Unless otherwise noted, all reactions were performed under the same conditions described in a representative example. [b] Isolated yield. No contamination of Δ^2-isomer was observed on NMR and IR in every case. All products were characterized by NMR, IR, and elemental analyses. [c] Yields based on NMR. [d] The reaction was carried out for 5 hr at room temperature. [e] The reaction was carried out for 5.3 hr at 7°C. [f] The starting material was recovered in >90% with CH_3CO_3H (4 eq) or m-CPBA (1 eq) at room temperature.

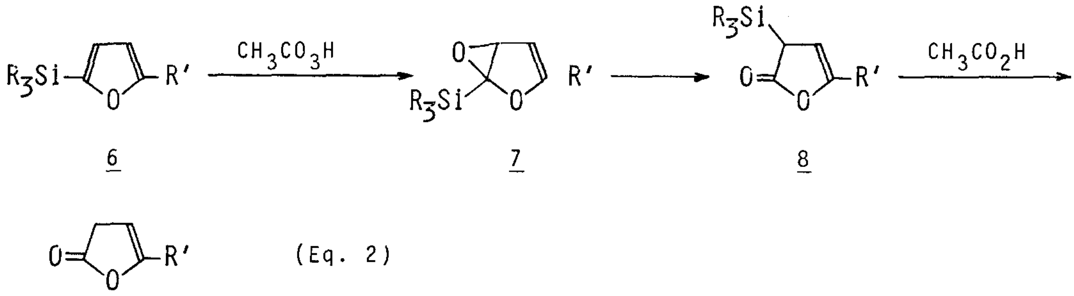
has been a report on peracid oxidation of a furan to a Δ^3-butenolide,[6) we could detect no Δ^3-butenolide and only intractable mixture was recovered upon oxidation of 2-hexylfuran with either peracetic acid or m-CPBA. Thus, trimethylsilyl group at the α-position of the furan ring is generally crucial to the clean formation of the corresponding Δ^3-butenolides.

Several features of this oxidation are further in order. In the first, the yield is slightly decreased with a furan possessing an olefinic moiety, probably due to its partial epoxidation (run 3). In a controlled experiment, 1-dodecene suffered epoxidation in ca. 15% yield under the standard reaction conditions employed here (CH_3CO_3H, NaOAc, CH_2Cl_2 at 7°C). Secondly, the presence of hydroxy group, especially at the furfuryl position, prevents a smooth conversion (runs 5 and 8). This difficulty can be circumvented by protecting as the t-butyldimethylsilyl ethers (runs 6 and 9). Finally, an electron-withdrawing substituent prevents an electrophilic attack of the peracid to recover most of the starting material even under forcing reaction conditions (run 10).

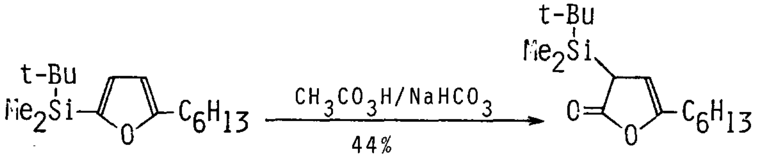
The following procedures are representative. To a stirred suspension of 40% peracetic acid[7) (380 mg, 2 mmol) and powdered anhydrous sodium acetate (50 mg) in methylene chloride (1.5 ml) was added 5-isopentyl-2-trimethylsilylfuran (105 mg, 0.5 mmol) in the same solvent (1.5 ml) at 0°C. After it was stirred for 3.5 hr at 7°C, aq $NaHCO_3$ and $Na_2S_2O_3$ solution was added and the aqueous layer was extracted with ether. The combined extracts were dried and concentrated to give an oil. Kugelrohr distillation afforded 4-isopentyl-Δ^3-butenolide (65∿70°(bath temp)/0.3 mmHg, 60 mg, 78%).

The mechanism of this reaction may be considered as shown in Eq 2. Epoxidation of 6 takes place selectively on the site bearing an electron-releasing trimethylsilyl group to yield 7, which undergoes C-O bond fission with concomitant migration of silyl group[8) to give 8 under acidic conditions.[9) In accord with this mechanism, we could isolate the intermediate 8 (R_3Si = t-Bu(Me)$_2$Si) in moderate yield (Eq 3). However, in the case of more acid-sensitive intermediates 8 (R_3Si = Me_3Si), we failed to isolate them, although their presence could be detected on NMR analysis of the reaction mixture in certain cases.

We are now studying further on application of this method to other substituted trimethylsilylfurans and on synthetic utilities of functionalized enol lactones.



(Eq. 2)



(Eq. 3)

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