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CHEMISTRY OF 2,5-BIS(TRIMETHYLSILOXY)FURANS.[1] III: SYNTHESIS OF γ-HYDROXYBUTENOLIDES.

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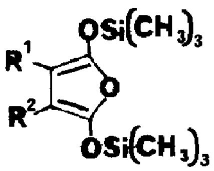
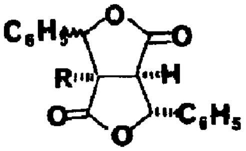
Summary: γ-Hydrobutenolides were obtained from the reaction of substituted 2,5-bis(trimethylsiloxy)furans with aldehydes and ketones using titanium tetrachloride activation. Similarly, α,β-unsaturated carbonyl compounds reacted as a Michael receptor with the title compounds to give γ-hydroxybutenolides.

In the preceeding paper we described the reaction of 2,5-bis(trimethylsiloxy)furan (1a) with aldehydes and ketones under activation of titanium tetrachloride. In all cases two molecules of the carbonyl compound reacted at the 3- and 4-positions of 1a, resulting in 3,7-dioxabicyclo[3.3.0]octane-4,8-diones (2, R = H)[1]. However, with increasing alkyl substitution in 1, a different reaction is observed: addition of the carbonyl compound to the 2-position. Thus 1b reacts with benzaldehyde and $TiCl_4$ to give an approximately equal mixture of the bis-lactone 2 (R = Me) (a 3:1 mixture of diastereoisomers), and the γ-hydroxybutenolide 3. It appears that the methyl group of 1b is sufficiently electron-donating to completely control the regioselectivity of



1

a; $R^1=R^2=H$
b; $R^1=Me$, $R^2=H$
c; $R^1=Ph$, $R^2=H$
d; $R^1,R^2=(CH_2)_4$
e; $R^1,R^2=CH_2CH=CHCH_2$



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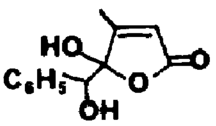

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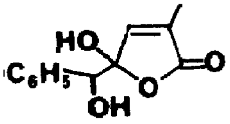

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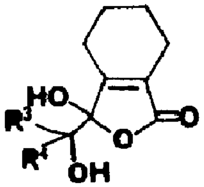
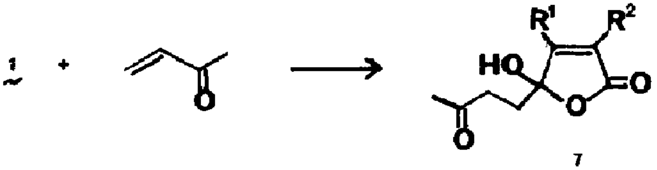


5 $R^3=Ph$, $R^4=H$
6 $R^3=R^4=Me$

addition, since none of the alternative 5-addition product 4 is produced[2].

Under the same conditions, the disubstituted furan 1d only reacted at the 2-position. With benzaldehyde it gave 5 (49%, mp 141-2°) and with acetone 6 (36%, mp 137-138.5°). Although compounds 3,5 and 6 could exist as a ring-open tautomer (5-hydroxy-4-oxo-2-enoic acids) or isomerize to a γ-oxo-δ-lactone (6H pyran-2,5-dione) no trace of these forms can be seen in the infra-red.

We have found that the 2,5-bis(trimethylsiloxy)furans 1b-e react at the 2-position with methyl vinyl ketone. The sole product is that of Michael addition to MVK, 7 (Table). This reaction occurs equally well under activatio



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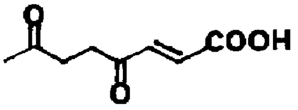

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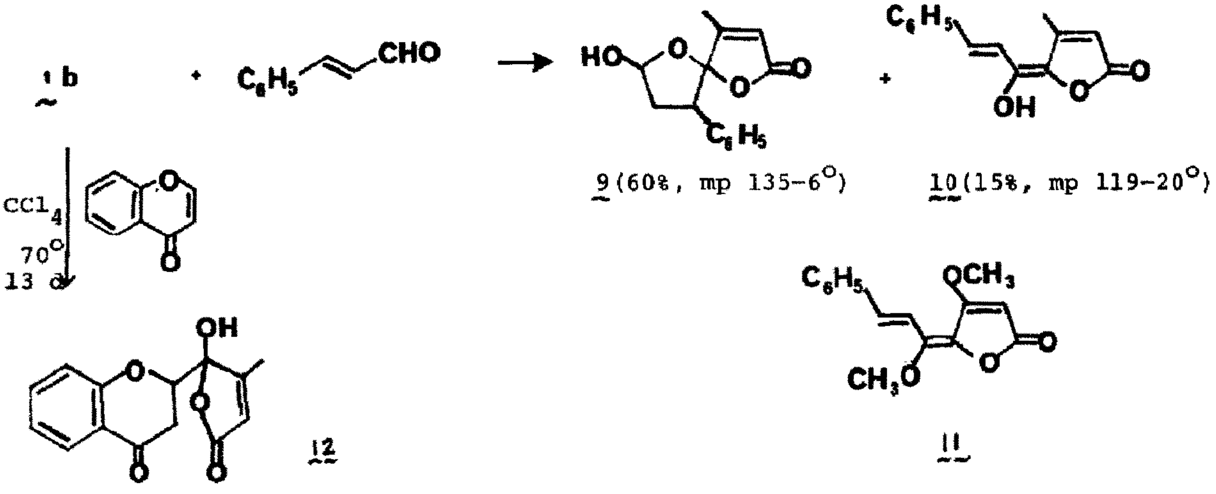
of titanium tetrachloride (CH_2Cl_2, -78°) or thermally (r.t. to 60°). The latt result is perhaps surprising in view of the facility with which compounds 1 undergo the Diels-Alder reaction with αβ-unsaturated esters[3], but appears to b fairly general with vinyl ketones (see below). The parent 2,5-bis(trimethylsiloxy)furan 1a also reacts with MVK, but gives 4,7-dioxoöct-2-enoic acid (8) in 55% yield. Presumably 8 arises by isomerization of the cis-isomer 7(R^1=R^2= during work-up.

TABLE

Cpd	Method	Yield %	mp
7 R^1=Me, R^2=H	$TiCl_4$, CH_2Cl_2, -78°,2 h	50	oil[7]
7 R^1=Ph, R^2=H	r.t., neat, 7 d	52	oil[7]
7 R^1,R^2=CH_2CH=$CHCH_2$	r.t., CCl_4, 3 d	99	96-7
8	$TiCl_4$,CH_2Cl_2, -78°, 3 h	55	113-4

Compound 1b also reacts under both thermal and $TiCl_4$-activated conditions with cinnamaldehyde, giving a 4:1 mixture of Michael (9) and aldol (10) additi products. The latter product is an analogue of the naturally - occurring methyl tetronate, piperolide (11).[4] Michael reaction at the 2-position of 1b wil even occur in good yield with deactivated vinyl ketones such as chromone t give 12, mp 180-2°, in 78% yield.

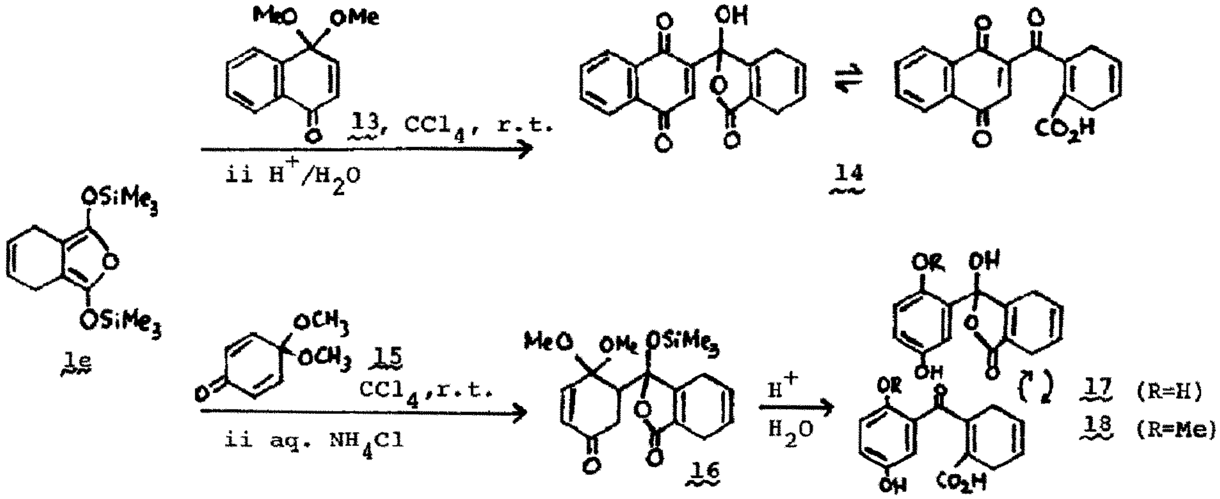
In contrast to the above results, neither a Michael addition nor a Diels-Alder reaction takes place between 1b and benzoquinone. Instead a rapi redox reaction gives hydroquinone bis(trimethylsilyl)ether and citraconic anhydride, an indication of the ease of oxidation of 1. This difficulty



9 (60%, mp 135-6°)   10 (15%, mp 119-20°)

12   11

can be overcome by using quinone acetals, which are easily prepared when the corresponding hydroquinone monomethyl ether is available[5]. Thus 1e reacted with naphthoquinone methyl acetal (13)[6] to produce 14 (51%, mp 218-220°d). It should be noted that 14 is a quinone; presumably the expected hydroquinone has



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1e   16   17 (R=H)   18 (R=Me)

undergone aerial oxidation during work-up. When benzoquinone methyl acetal (15)[5] was used, the initial Michael addition product 16 was isolated; this was unstable and decomposed on standing (or more rapidly on acidic hydrolysis) to the hydroquinone 17 (49%, mp 208-210°d) and its methyl ether 18 (15%, gum[7]). Compounds 14, 17 and 18 are evidently an equilibrium mixture of cyclic and open tautomers, as i.r. bands corresponding to both forms are observed. Interconversion must be rapid on the nmr timescale, since only one set of peaks is observed.

γ-Hydroxybutenolides have previously been prepared by oxidation of furans[8], condensation of α-ketoacid derivatives with carbonyl compounds[8] or by reaction of maleic anhydrides with Grignard reagents[8,9]. The present route involves conceptually the umpolung of the anhydride moiety with the γ-position having donor property[10]. In this light, the easy construction of 8 should be compared with the several syntheses of pyrenophorin[11-15] concerning construction of the same carbon skeleton.

The application of 2,5-bis(trimethylsiloxy)furans to the synthesis of natural products will be further explored in our laboratories.

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