

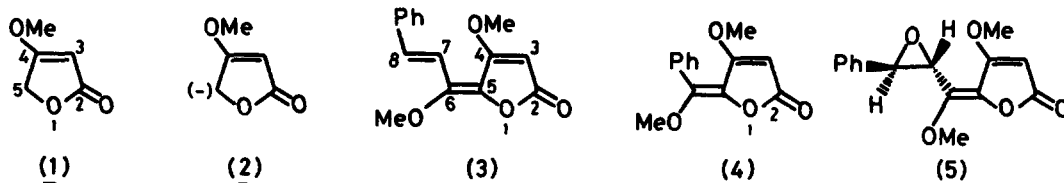
2-TRIMETHYLSILYLOXY-4-METHOXYFURAN. AN EXCELLENT SYNTHON FOR THE  
PRODUCTION OF 5-SUBSTITUTED TETRONATES (4-METHOXYBUTENOLIDES).

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The preparation of 2-trimethylsilyloxy-4-methoxyfuran (6) is described. Under the influence of Lewis acids, this compound is substituted by a wide variety of reagents in a regiospecific fashion at C-5 to give substituted methyl tetronates. Its utility is exemplified by syntheses of fadyenolide and 7,8-*trans*-epoxy-5,6-dihydropiperolide. In addition (6) reacts with facility in the Diels-Alder reaction and has the potential of yielding many resorcinol derivatives.

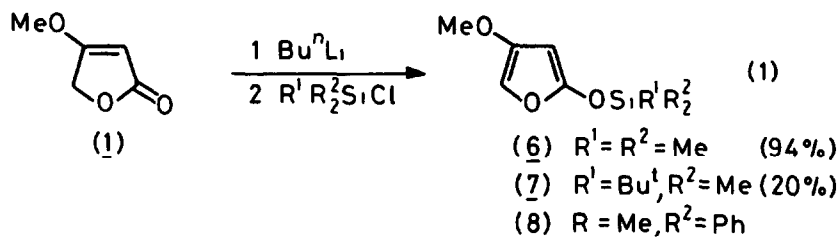
We have previously introduced the synthon (1) as a readily available substance which can be substituted at C-5 using the anion (2)<sup>1</sup>. In this way we have synthesised<sup>1,2</sup> both piperolide<sup>3</sup> (3) and fadyenolide (4)<sup>2</sup>.



However in order to produce rather more sensitive materials such as epoxy-piperolide (5)<sup>4</sup>, we required a synthetic equivalent of (2) that could be used in non-basic conditions. We therefore turned to trimethylsilylketene acetals of the type previously used by Asoaka<sup>5</sup> and Chan<sup>6</sup>. Indeed a very recent report<sup>7</sup> on the use of 2-trimethylsilyloxyfuran for the production of ylidenebutenolides prompts us to a preliminary report of our work with 2-trimethylsilyloxy-4-methoxyfuran (6) as a highly efficient equivalent of anion (2) which can be utilised for the synthesis of a wide variety of 5-substituted methyl tetronates (3-methoxybutenolides).

The ketene acetal (6) was readily prepared from (1) in 94% yield,\* as shown in Eq 1. As (6), b.p. 80-82°C/12mm., is extremely susceptible to hydrolysis it was distilled directly from the reaction mixture after removal of solvent.

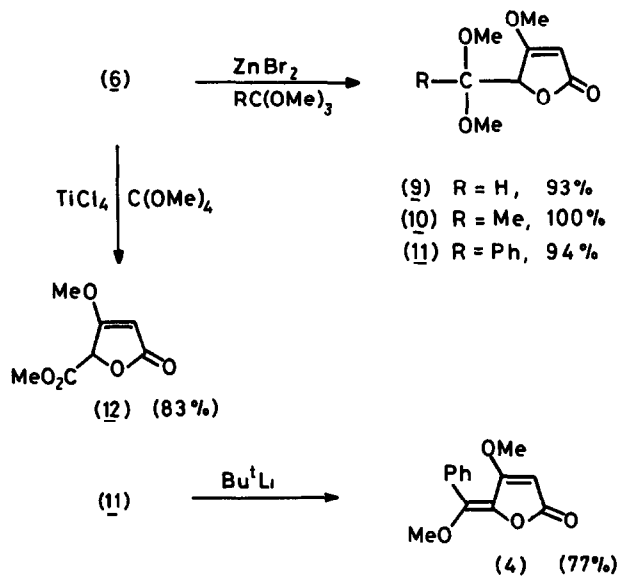
\* In all cases, yields are of isolated, fully characterised products.



The *t*-butyl derivative (7) was more stable to hydrolysis but could not be prepared efficiently, whilst we could not obtain (8) at all

We therefore used (6) as our anion equivalent. Unless otherwise stated all reactions were carried out in methylene dichloride at low ( $-100^\circ\text{C} \rightarrow -78^\circ\text{C}$ ) temperatures in the presence of catalytic amounts of either  $\text{ZnBr}_2$  or  $\text{TiCl}_4$ . Attempts to use  $\text{Bu}_4^{\text{n}}\text{NF}$  led to complex products and were abandoned. In all cases the substitution reactions were regiospecific in that only C-5 was attacked, no reaction being seen at C-3

(A) Reactions with ortho-esters



Scheme 1

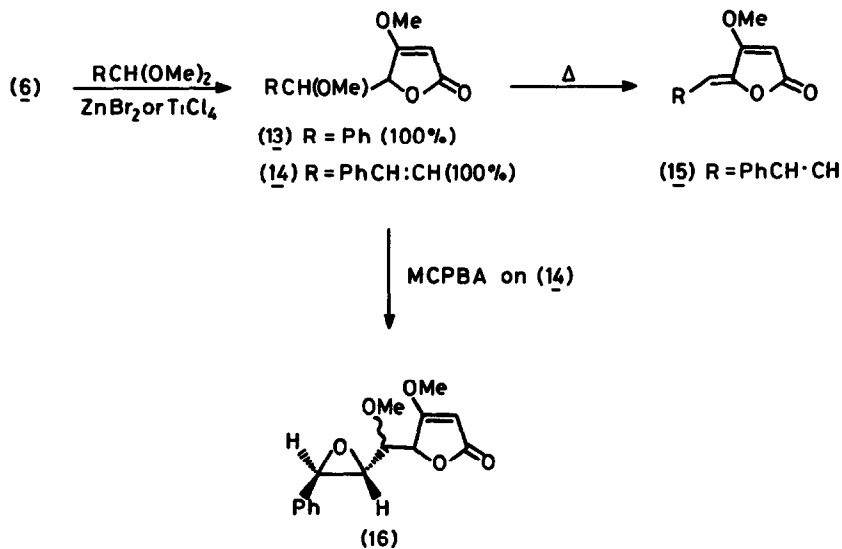
These reactions were of particular interest to us as elimination of methanol from the products leads directly to 4,6-dimethoxy-ylidenenbutenolides of the fadyenolide and piperolide series. In every case reaction proceeded smoothly to yield acetals (9) - (11) in the yields shown (Scheme 1). In the case of (11) attempts to eliminate methanol under a wide variety of acid conditions failed but treatment with  $\text{Bu}^t \text{Li}$  (not  $\text{Bu}^{\text{n}} \text{Li}$  or  $\text{Bu}^{\text{sec}} \text{Li}$ ) gave *Z*-fadyenolide in 77% yields, the whole process from (1) being short and efficient. The use of  $\text{Bu}^t \text{Li}$  to effect elimination from acetals such as (9) - (11) is general and will be

exemplified in our full paper

When (6) was reacted with  $C(OMe)_4$ , only carbomethoxy-4-methoxybutenolide (12) resulted and so far we have been unable to isolate the corresponding ortho-ester which is presumably the first reaction product.

(B) Reactions with acetals.

The use of acetals allows for the production of ylidenebutenolide unsubstituted at C-6<sup>1</sup> (Scheme 2)

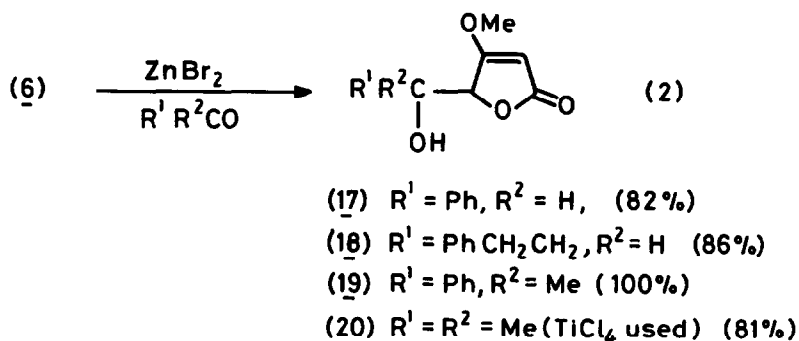


Scheme 2.

Reactions proceed quantitatively with either acetal used (Scheme 2) to yield the methyl ethers (13) and (14). Simply heating (14) causes elimination of methanol to give (15), whilst its oxidation with *m*-chloroperbenzoic acid yields 7,8-trans-epoxy-5,6-dihydropiperolide (16) as an erythro, threo mixture.

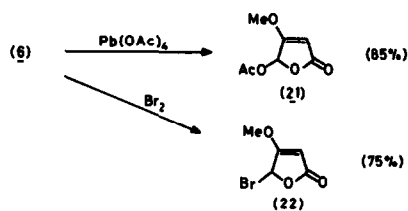
(C) Reactions with Aldehydes and Ketones.

These reactions also proceed in a regioselective fashion with high yields (Eq 2). As with the acetals, mixtures of erythro- and threo- compounds result, in the appropriate cases.

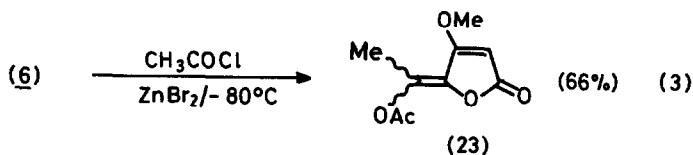


(D) Miscellaneous Reactions

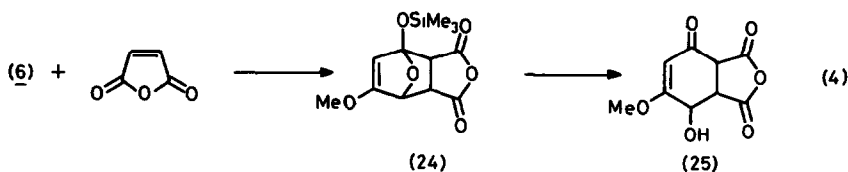
Lead tetraacetate and bromine react directly with (6) to give the corresponding 5-substituted compounds (21) and (22). Both (21) and (22) are useful synthons.



Reactions of (6) with acyl halides led generally to complex mixtures. However when acetyl chloride was used as solvent and  $\text{TiCl}_4$  as catalyst, reaction occurred at  $-80^\circ\text{C}$  to give a good yield of the enol acetate (23) as a *E*, *Z*-mixture (Eq 3).



As would be expected, furan (6) is a highly effective diene in the Diels-Alder reaction and interacted exothermically with maleic anhydride. The intermediate oxide (24) was very labile and rapidly yielded the crystalline adduct (25) in >80% yield (Eq 4). Thus (6) should be an excellent intermediate for the production of resorcinol derivatives, and this is currently under investigation.



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