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γ -KETO ESTERS AND γ -BUTYROLACTONES
FROM THE REACTION OF DIALKOXYDIHYDROFURANS
WITH TRIMETHYLSILYL IODIDE

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Abstract: Dimethoxydihydrofurans are converted into γ -keto esters and γ -butyrolactones by a new procedure using an equimolar quantity and an excess of trimethylsilyl iodide, respectively.

The synthesis of 1,4-dicarbonyl compounds, useful precursors for various cyclopentenone derivatives, has been widely developed¹. The recent report by Suzuki and co-workers² on the conversion of dialkoxydihydrofurans into γ -keto esters using a ruthenium hydride catalyst, has prompted us to describe our results on the mild formation of γ -keto esters from dialkoxydihydrofurans and in-situ prepared trimethylsilyl iodide (TMSI).

Applications of TMSI as a Lewis acid catalyst and as a reagent for cleavage of acetals, ketals and esters are well documented^{3,4}. Unexpectedly, however, when we used TMSI in the deprotection of the carbonyl functionalities in monoalkyl-substituted dimethoxy-

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dihydrofurans, we observed the formation of γ -keto esters as the major reaction products. Thus, when 2-methyl-2,5-dimethoxy-2,5-dihydrofuran (1b, mixture of *cis*- and *trans*-isomers) was treated with an equimolar quantity of TMSI for 15 minutes and subsequently hydrolysed, ^1H NMR analysis revealed methyl 4-oxo-pentanoate (2b) to be the major product (77 %), with γ -butyrolactone (3b) as a by-product (approximately 20 % yield). The γ -keto ester was easily isolated by chromatography or distillation although these techniques gave rise to some conversion of 2b into 3b. The γ -butyrolactone was obtained as the main product when an excess of TMSI (≥ 3 equiv.) was used.

The conversion of dialkoxydihydrofurans into γ -keto esters is outlined in Scheme 1. The results of the reactions of a number of dimethoxydihydrofurans with TMSI are summarized in Table 1⁵.

Dimethoxydihydrofurans are conveniently prepared from substituted furans^{6,7} and their mild reaction with TMSI constitutes a

Scheme 1

Table 1: γ -Keto esters and γ -butyrolactones via rearrangements of 2,5-dimethoxydihydrofurans using TMSI⁹

Dimethoxydihydrofuran	γ -Keto ester ^{a)}	γ -Butyrolactone ^{b)}
<u>1</u>	<u>2</u> (yield, %) ^{c)}	<u>3</u> (yield, %)
<u>a</u> R = H	R = H , -	R = H , 27
<u>b</u> R = CH ₃	R = CH ₃ , 53(77)	R = CH ₃ , 84
<u>c</u> R = C ₂ H ₅	R = C ₂ H ₅ , 28(42)	R = C ₂ H ₅ , 54
<u>d</u> R = CH ₂ CH ₂ COCH ₃	R = CH ₂ CH ₂ COCH ₃ , 51	-
<u>6</u>	<u>7</u>	

a) using 1.1 equiv. of TMSI

b) using 3.0 equiv. of TMSI

c) isolated yield (yields by NMR)

d) unidentified by-product (no methyl ester formed)

useful alternative to the conventional methods for the preparation of γ -keto esters (2) and γ -butyrolactones (3).

The product formation can be explained by TMSI-catalysed double-bond migration in 1 and subsequent deketalization, followed either by hydrolysis to yield 2 or by lactonization under the influence of excess TMSI to yield 3. The conversion of 1 does not proceed through γ -methoxy- γ -butyrolactones as these compounds were found not to be affected by TMSI under the conditions used⁸.

Scheme 2

Besides the above-described route to γ -keto esters we found that γ -butyrolactones 5, which are easily accessible via photooxidation of furans, followed by dehydration with lead tetraacetate⁷, can be converted into γ -keto esters in high yield (2b, 87 %; 2c, 75-85 %) using magnesium in methanol (Scheme 2). This conversion involves a reduction of the conjugated double-bond followed by esterification with methanol.

Methyl 4-oxopentanoate from 1b using TMSI:

A mixture of 0.73 g (4.4 mmol) of KI and 0.47 g (0.59 ml, 4.4 mmol) of trimethylsilyl chloride in 20 ml of dry acetonitrile containing 0.5 g of molecular sieves (4A) was stirred at room temperature for 15 minutes under a nitrogen atmosphere. Subsequently, a solution of 0.57 g (4.0 mmol) of 2-methyl-2,5-dimethoxydihydrofuran (1b) in 5 ml of acetonitrile was added and the resulting brown mixture stirred for an additional 15 minutes. Hydrolysis with 100 ml of water at room temperature for 90 minutes was followed by extraction with diethyl ether (2x50 ml). The ether solution was washed with Na₂CO₃ solution (30 ml), Na₂S₂O₄ solution (2x25 ml) and saturated NaCl solution (30 ml) and dried over MgSO₄. After removal of the solvent by distillation the remaining oil was

chromatographed over silica gel (with CH_2Cl_2 as eluent) to give 0.27 g (53 %) of pure 2b as an oil⁵. ^1H NMR (CDCl_3) δ = 2.14 (s, 3 H), 2.60 (m, 4 H), 3.66 (s, 3 H); ^{13}C NMR (CDCl_3) δ = 27.6, 29.7, 37.8, 51.6, 173.0, 206.5.

Methyl 4-oxopentanoate from 5b using Mg in CH_3OH

To 0.19 g (8.0 mmol) of magnesium (Grignard grade) in 20 ml of methanol, 0.80 g (6.2 mmol) of γ -methoxybutyrolactone 5b was added and the resulting mixture was stirred at 10-15 °C for 3 hours. To the slightly yellow slurry obtained 10 ml of 2 N HCl solution was added and after stirring for an additional 5 minutes 100 ml of diethyl ether and 25 ml of saturated aqueous NaCl solution were added. The organic layer was separated and washed, first with aqueous Na_2CO_3 until neutral, and then with a saturated NaCl (25 ml) solution. After drying over MgSO_4 and removal of the solvent by distillation a yellow oil was obtained; flash chromatography over silica gel (CH_2Cl_2) afforded 0.70 g (87 %) of pure 2b.

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5. γ -Keto esters and lactones were fully characterized by spectroscopic means and were prepared by independent methods. Spiro lactone 7 was identical to a sample prepared by photooxidation of 2-furylbutanol-2⁷. We do not have a satisfactory explanation for the reaction of 6 with TMSI.
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8. The selectivity of the reaction with dimethoxydihydrofurans is remarkable as the dimethoxyacetals of α,β -unsaturated aldehydes such as acrolein and β -phenylacrolein yielded complex product mixtures in their reactions with TMSI.
9. Deketalization is the major reaction of 2,5-disubstituted 2,5-dimethoxydihydrofurans e.g. 2,5-dimethyl-2,5-dimethoxydihydrofuran gives 3-penten-2,5-dione in 82 % yield.