

**Functionalization with Silyl Enol Ethers, VI [1]
Zinc Chloride Mediated Alkoxyalkylation
of O-Methyl-O-(trimethylsilyl) Keten Acetals with
2-Alkoxy-1,3-dioxolanes**

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O-Methyl-O-(trimethylsilyl) keten acetals **2** were regioselectively alkoxyalkylated by 2-alkoxy-1,3-dioxolanes **1** in the presence of zinc chloride. This method represents a good way for synthesis of α -protected β -keto carbonic esters **4**.

(Keywords: Alkoxyalkylation of (trimethylsilyl) keten acetals, with $\text{ZnCl}_2 \cdot \text{Et}_2\text{O}$ as Lewis-acid)

Funktionalisierung mit Silylenolethern, VI[1]. Zinkchlorid-induzierte Alkoxyalkylierung von O-Methyl-O-(trimethylsilyl)keten-acetal mit 2-Alkoxy-1,3-dioxolan

O-Methyl-O-(trimethylsilyl)keten-acetale wurden mit 2-Alkoxy-1,3-dioxolanen **1** in Gegenwart von Zinkdichlorid regioselektiv alkoxyalkyliert. Dieses Verfahren stellt einen guten Weg zur Gewinnung von α -geschützten β -Ketokarbonsäureestern **4** dar.

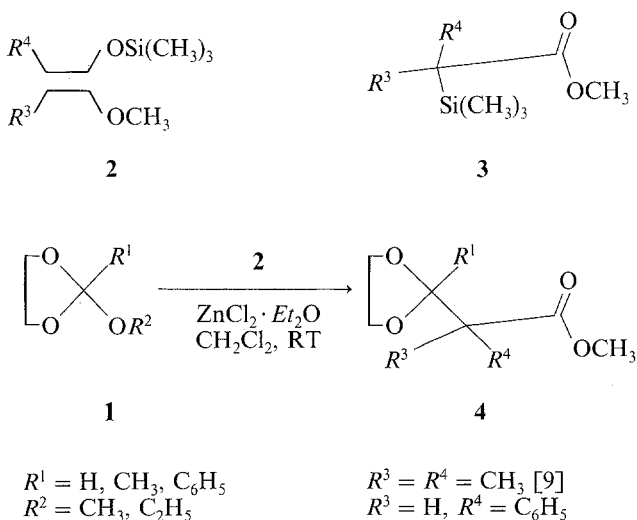
Introduction

Regioselective alkoxyalkylation of silyl enol ethers and derivatives play an important role in synthon chemistry for synthesis of natural products and other complex molecules [2, 3]. In our work we introduced protected acyl units from orthoester in silyl enol ethers and have synthesized many regioselectively protected 1,3- and 1,5-diketones, which are interesting precursors for further functional group transformations. Within this methodology there should be also a great interest to obtain α -protected β -keto carboxylic acid derivatives. These are also very important intermediates for the preparation of a variety of natural products [4, 5, 6 a, b].

Results and Discussions

O-Alkyl-O-(trialkylsilyl) keten acetals **2** and 2-(trialkylsilyl) carbonic esters **3** are used very commonly as d^2 -synthons in synthetic organic chemistry for carbon-carbon bond formation [6 a-d]. Among the various methods, the most important one for their synthesis is the O- or C-silylation of esters with trimethylsilyl triflate [7] (for a further method see Ref. [6 c]). Carbonic esters with $-M$ -effects substituents at the α -position were smoothly O-silylated in the presence of triethylamine, forming O-alkyl-O-(trimethylsilyl) keten acetals **2**. Also carbonic esters which bear $+I$ -effect substituents at the α -position, are partly O-silylated by this method, but the d^2 -analogous α -(trialkylsilyl) carbonic esters **3** are generally main products of this reaction [7].

The d^2 -synthon **3** ($R^3 = H, CH_3$, $R^4 = H, CH_3$) does not react with the a^1 -reagents 2-alkoxy-1,3-dioxolanes **1** using different *Lewis* acids like $ZnCl_2 \cdot Et_2O$, $BF_3 \cdot Et_2O$ or $TiCl_4$ [8 a] in our studies. Fail of al-



4	R^1	R^2	R^3
4a	H	CH ₃	CH ₃
4b	CH ₃	CH ₃	CH ₃
4c	C ₆ H ₅	CH ₃	CH ₃
4d	H	H	C ₆ H ₅
4e	CH ₃	H	C ₆ H ₅
4f	C ₆ H ₅	H	C ₆ H ₅

koxy methylation should be connected with the character of the Si—C bond of **3**, because for C—C bond formation heterolytic breakage of Si—C bond of **3** is necessary, which does not occur under this reaction conditions. In contrast to this the silyl keten acetal **2*** reacts in dichloromethane with the S_N1 -active acylation equivalents **1** by $ZnCl_2 \cdot Et_2O$ -catalysis to the α -protected β -ketoesters **4** (yield 26–94%) smoothly and regioselectively. The reaction in this case should proceed under the control of the frontier orbitals [10]. The 1,3-Dioxolenium-ion which is generated from **1** by $ZnCl_2$ -catalysis, attacks the α -position of **2**, subsequently Cl^- -mediated desilylation affords the products **4** [2].

It is noteworthy to remark, that the carbon-carbon bond formation on **2** was not influenced by bulky groups as dimethyl or phenyl at the reaction centers of the reactants [8 b]. These present results are generally in good agreement with our earlier studies, which confirm that $ZnCl_2 \cdot Et_2O$ in dichloromethane is the best catalyst for this aldol type reaction [1]. Hence with these experiments, we have demonstrated a further example of regioselective alkoxyalkylation of silyl enol ether derivatives which are certainly capable of further experimental application for deriving selectively protected dicarbonyl compounds as useful building blocks.

The constitutions of the α -dioxolanyl carbonic methyl esters **4** were proved unambiguously by spectroscopic data and elemental analyses.

Experimental

Melting points (uncorrected): Mettler FP5, Büchi 510. IR-Spectra: Perkin-Elmer 177, 1H -NMR-spectra: Varian T60 (δ -Skala), Mass-spectra: LKB, CHN-Mikroanalysis: Perkin-Elmer 240 C, Elemental Analyzer.

O-Methyl-O-(trimethylsilyl) keten acetal (**2**) and α -(Trimethylsilyl) ester (**3**) were synthesised according to Ref. [7].

General Method for the Synthesis of α -1,3-Dioxolanyl esters 4

To a solution of 10 mmol **1** and 10 mmol **2** in 25 ml anhydrous dichloromethane, 5 mmol, $ZnCl_2 \cdot Et_2O$ were dropped via a glass syringe at room temperature under N_2 -atmosphere. The reaction mixture was stirred for 1 h, then quenched with saturated sodium hydrogen carbonate. The products were extracted with dichloromethane three times. The extracts were dried over anhydrous sodium sulfate, then dichloromethane was evaporated and the remaining residue was chromatographed through a column filled with silica gel 60 (Fluka AG; *EtOAc/n*-Hexan). The percent yields of products, the elemental and spectroscopic data are given in Tables 1 and 2.

* Which possesses in general a higher nucleophilic reactivity as silyl enol ethers [8 b].

Table 1. Yields and analytical data of α -1,3-dioxolanylestere 4a-f

Product	m.p. [°C]	% Yield	Molecular weight	Anal. C%	H%
2-(1,3-Dioxolane-2-yl)-2,2-dimethyl-methyl ester (4a)	oil	47	C ₈ H ₁₄ O ₄ (174.2)	calcd. 55.16 found 54.91	8.10 8.07
2-(2-Methyl-1,3-dioxolane-2-yl)-2,2-dimethyl-methyl ester (4b)	oil	51	C ₉ H ₁₆ O ₄ (188.2)	calcd. 57.43 found 57.37	8.56 8.36
2-(2-Phenyl-1,3-dioxolane-2-yl)-2,2-dimethyl-methyl ester (4c)	76-77	26	C ₁₄ H ₁₈ O ₄ (250.3)	calcd. 67.18 found 67.05	7.24 7.25
2-(1,3-Dioxolane-2-yl)-2-phenyl-methyl ester (4d)	oil	94	C ₁₂ H ₁₄ O ₄ (222.2)	calcd. 64.85 found 64.36	5.44 5.14
2-(2-Methyl-1,3-dioxolane-2-yl)-2-phenyl-methyl ester (4e)	62.6	71	C ₁₃ H ₁₆ O ₄ (236.26)	calcd. 66.08 found 65.90	6.82 6.81
2-(2-Phenyl-1,3-dioxolane-2-yl)-2-phenyl-methyl ester (4f)	89.3	68	C ₁₈ H ₁₈ O ₄ (298.33)	calcd. 72.46 found 73.06	6.08 6.50

Table 2. IR- and ¹H-NMR data of 4a-f

No.	IR [cm ⁻¹] ν _c = 0	¹ H-NMR (CDCl ₃ , TMS)
4a	1 725	1.17 (s, 6H, 2 × CH ₃), 3.67 (s, 3H, OCH ₃), 3.9 (s, 4H, CH ₂ -ring), 5.06 (s, 1H, CH)
4b	1 725	1.2 (s, 6H, 2 × CH ₃), 1.34 (s, 3H, CH ₃), 3.67 (s, 3H, OCH ₃), 3.93 (s, 4H, CH ₂ -ring)
4c	1 725	1.23 (s, 6H, 2 × CH ₃), 3.6 (s, 3H, OCH ₃), 3.63-4.16 (m, 4H, CH ₂ -ring), 7.13-7.46 (m, 5H, arom. H)
4d	1 735	3.7 (s, 3H, OCH ₃), 3.76-3.93 (m, 5H, CH ₂ -ring + 1 CH), 5.43 (d, 1H, J = 7 Hz, CH), 7.33 (s, 5H, arom. H)
4e	1 735	1.36 (s, 3H, CH ₃), 3.66 (s, 3H, OCH ₃), 3.73-4.0 (m, 5H, CH ₂ -ring + 1 CH), 7.0-7.56 (m, 5H, arom. H)
4f	1 735	3.52 (s, 3H, OCH ₃), 3.6-3.92 (m, 4H, CH ₂ -ring), 4.18 (s, 1H, CH), 7.0-7.5 (m, 10H, arom. H)

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