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$TiCl_4$ and $LiClO_4$ Promoted Additions of *O*-Silylketene Acetals to Chiral β-Formyl Esters

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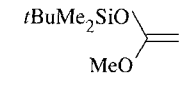
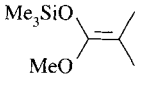
Abstract. Lewis acid promoted additions of *O*-silylketene acetals **1a** and **1b** to β-formyl ester **2** furnished γ-lactones **3a** and **3b**. Employing $TiCl_4$ as promotor chelate control leads to moderate or excellent *trans* selectivity, whereas $LiClO_4$ as Lewis acid did not induce appreciable diastereoselectivity.

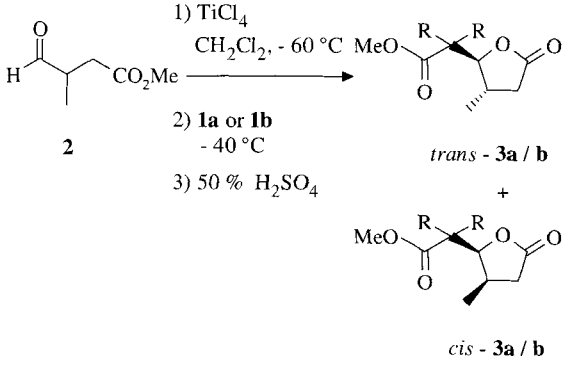
Recently we reported our results concerning the Mukaiyama reaction of silyl enol ethers with chiral β-formyl carboxylates such as **2** which provided functionalized γ-lactones [2]. The preferential formation of *trans* isomers in the presence of $TiCl_4$ was explained by chelate control with the ester function of **2** serving as ligand [3]. In continuation of this study we present our results when *O*-silylketene acetals **1a** and **1b** were employed as nucleophiles. These allowed also the use of lithium perchlorate as Lewis acid which had been introduced as promotor of several reactions quite recently [4]. Reetz *et al.* [5] could demonstrate that $LiClO_4$ also promotes additions of *O*-silylketene acetals to aldehydes.



1a



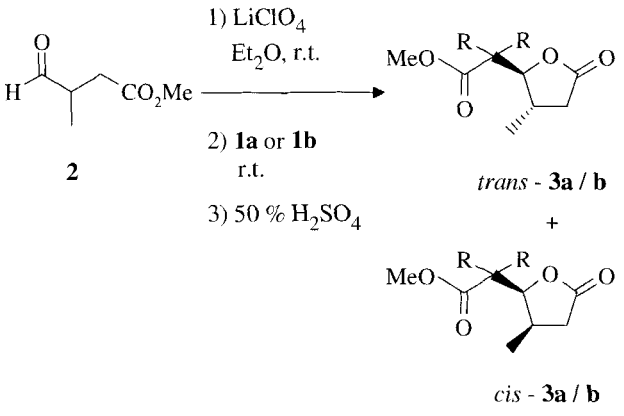
1b



a	R = H	83%	*trans* : *cis* = 67:33
b	R = Me	93%	*trans* : *cis* = 97:3

Employing standard conditions for $TiCl_4$-induced additions as developed for the additions of silyl enol ethers to **2** the reaction of *O*-silylketene acetal **1a** provided the expected γ-lactone **3a** after acidic workup with a moderate *trans/cis* selectivity. Interestingly, this selectivity increased to as much as 97:3 when the sterically more demanding nucleophile **1b** was combined with **2**. Both reactions proceeded with very good yield. These results are in agreement with the interpretation of other reactions of **2** with Lewis acidic organometallics: a seven-membered ring chelate of the Lewis acid and **2** is attacked by the nucleophile *anti* to the methyl group of **2** thus affording *trans* γ-lactones with preference. The remarkably higher selectivity of **1b** may be explained by the enhancement of steric effects due to the two additional methyl groups at the nucleophilic centre. However, this effect is probably superposed by an *intrinsic trans* selectivity of the reactions of silylated nucleophiles bearing one or two alkyl groups at the bond forming carbon atom (see below).

The $LiClO_4$-promoted reactions of **1a** and **1b** with β-formyl carboxylate **2** proceeded with moderate yields and low diastereoselectivities. Whereas **3a** was formed with low *cis* preference the corresponding reaction leading to the geminally dimethyl substituted γ-lactone **3b** was moderately *trans* selective.



a	R = H	54%	*trans* : *cis* = 45:55
b	R = Me	48%	*trans* : *cis* = 67:32

The result with **1a** can clearly be taken as evidence that chelate control is not operating under these conditions. This was unexpected since reactions of cuprates with **2** proceeded with excellent *trans* selectivity [6]. For these transformations we suggested seven-membered chelates with the lithium cation as bridging Lewis acid as interpretation. Also, we presume that it is not chelate control but the intrinsic higher *trans* selectivity of terminally substituted nucleophiles which slightly favours formation of *trans*-**3b** over *cis*-**3b**.

In summary, our results with *O*-silylketene acetals **1** demonstrate that similar rules govern their additions to β-formyl carboxylates such as **2** under $TiCl_4$ promotion as the reactions with other nucleophiles. In certain cases very high diastereoselectivities can be achieved furnishing *trans*-γ-lactones that may be suitable for further synthetic transformations. $LiClO_4$ is apparently not able to form chelates with **2** thus leading to low diastereoselectivities.

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Experimental

For general information see [2b]
Starting materials: **1a** [7], **1b** (Fluka, 95%), **2** [8]

$TiCl_4$ Promoted Additions

4,5-Dihydro-5-(methoxycarbonylmethyl)-4-methyl-2(3H)-furanone (**3a**)

To a solution of 0.260 g (2.00 mmol) **2** in 10 ml of dichloromethane was added 0.379 g (2.00 mmol) of $TiCl_4$ at –60 °C. The mixture was warmed up to –40 °C within 15 min and 0.565 g (3.00 mmol) of **1a**, dissolved in 7 ml of dichloromethane, was slowly added. After 1 h at – 40 °C 50% aqueous sulfuric acid (2 ml) was added, the cooling bath was removed and the mixture was stirred for 30 min. Extractive workup (H_2O/CH_2Cl_2), drying (Na_2SO_4), and evaporation of solvent provided 0.559 g crude product which was purified by chromatography on silica gel 60 (hexane/ethyl acetate, 1:1) to give 0.285 g (83%) of **3a** as colourless liquid (*trans*:*cis* = 67:33 according to GC). – ^1H NMR ($CDCl_3$, 200 MHz): δ 4.86 (td, *J* = 6, 8 Hz, 0.33 H, *cis*-5-H), 4.40 (q, *J* = 6.5 Hz, 0.67 H, *trans*-5-H), 3.65 (s, 3 H, CO_2CH_3), 2.67–2.46, 2.40–2.05 (2 m, 5 H, 3-H, 4-H, 5-CH), 1.10 (d, *J* = 6.5 Hz, 2.01 H, *trans*-4-CH_3), 0.95 (d, *J* = 7 Hz, 0.99 H, *cis*-4-CH_3). – ^{13}C NMR ($CDCl_3$), *trans*-Isomer: δ 175.4 (s, C-2), 170.0, 51.8 (s, q, CO_2CH_3), 82.4 (d, C-5), 38.4, 36.4 (2 t, C-3, 5-C), 35.5 (d, C-4), 17.2 (q, 4-CH_3). *cis*-Isomer: δ 175.7 (s, C-2), 170.1, 51.8 (s, q, CO_2CH_3), 78.7 (d, C-5), 36.8, 34.8 (2 t, C-3, 5-C), 32.4 (d, C-4), 13.9 (q, 4-CH_3). – IR (Film): ν = 2960 cm^{-1}, 2940, 2870, 2830 (C-H), 1780 (C=O, Lactone), 1740 (C=O, Ester).

$C_8H_{12}O_4$	Calcd.:	C 55.80	H 7.02
(172.2)	Found:	C 55.70	H 7.31.

4,5-Dihydro-5-(1-methoxycarbonyl-1-methylethyl)-4-methyl-2(3H)-furanone (**3b**)

Analogous to the synthesis of **3a** reaction of **2** (0.260 g, 2.00 mmol), $TiCl_4$ (0.379 g, 2.00 mmol), and **1b** (0.523 g, 3.00 mmol) provided after Kugelrohr distillation (70 °C/0.04 Torr) 0.374 g (93%) of **3b** as colourless liquid (*trans*:*cis* = 97:3 according to GC). – ^1H NMR ($CDCl_3$, 200 MHz), *trans*-Isomer: δ 4.29 (d, *J* = 5 Hz, 1 H, 5-H), 3.71 (s, 3 H, CO_2CH_3), 2.76 (dd, *J* = 9.5, 18 Hz, 1 H, 3-H), 2.57–2.34 (m, 1 H, 4-H), 2.18 (dd, *J* = 6, 18 Hz, 1 H, 3-H), 1.27, 1.22 (2 s, 3 H each, CH_3), 1.18 (d, *J* = 7 Hz, 3 H, 4-CH_3). *cis*-Isomer: δ 4.71 (d, *J* = 6.5 Hz, 1 H, 5-H), 3.73 (s, 3 H, CO_2CH_3), 2.96–2.59 (m, 2 H, 3-H, 4-H), 2.22 (dd, *J* = 6.5, 17 Hz, 1 H, 3-H), 1.36, 1.26 (2 s, 3 H each, CH_3), 1.06 (d, *J* = 7 Hz, 3 H, 4-CH_3). – ^{13}C NMR ($CDCl_3$), *trans*-Isomer: δ 176.1 (s, C-2), 175.2, 52.0 (s, q, CO_2CH_3), 90.8 (d, C-5), 46.1 (s, 5-C), 36.8 (t, C-3), 30.6 (d, C-4), 21.6, 20.9, 20.1 (3 q, CH_3). *cis*-Isomer: δ 176.2 (s, C-2), 175.7, 52.0 (s, q, CO_2CH_3), 85.8 (d, C-5), 45.1 (s, 5-C), 37.3 (t, C-3), 33.4 (d, C-4), 25.6, 19.5, 14.4 (3 q, CH_3). – IR (Film): ν = 2980 cm^{-1}, 2955, 2880 (C-H), 1780 (C=O, Lactone), 1735 (C=O, Ester).

$C_{10}H_{16}O_4$	Calcd.:	C 59.98	H 8.05
(200.2)	Found:	C 59.97	H 8.15.

$LiClO_4$ Promoted Additions

Synthesis of **3a**: A mixture of 5.32 g (50.0 mmol) of $LiClO_4$ and of 10 ml of diethyl ether was stirred for 1 h. To the resulting solution were added 0.260 g (2.00 mmol) of **2** and after 15 min at room temp. 0.565 g (3.00 mmol) of **1a**. After stirring for 15 min at room temp. the mixture was hydrolyzed with 2 ml of 50% aqueous sulfuric acid, stirred for 30 min, than diluted with 20 ml of water and extracted with diethyl ether (5×20 ml). Extraction of the combined organic layers with saturated aqueous $NaHCO_3$ solution (30 ml) and saturated aqueous NaCl solution (30 ml), drying (Na_2SO_4) and evaporation of solvent furnished the crude product which was purified by chromatography: 0.186 g (54%) of **3a** (*trans* : *cis* = 45:55 according to GC).

Synthesis of **3b**: Analogous to the preparation of **3a** reaction of **2** (0.260 g, 2.00 mmol), $LiClO_4$ (5.32 g, 50.0 mmol in 10 ml of diethyl ether), and **1b** (0.523 g, 3.00 mmol) afforded after purification by Kugelrohr distillation (90 °C/0.2 Torr) 0.193 g (48%) of **3b** (*trans*:*cis* = 63:37 according to GC).

References

[1] H. Angert, Dissertation, Technische Universität Dresden 1995

[2] a) H. Angert, T. Kunz, H.–U. Reißig, Tetrahedron **48** (1992) 5681; b) H. Angert, R. Czerwonka, H.–U. Reißig, Liebigs Ann. **1996**, 259; c) H. Angert, R. Schumacher, H.–U. Reißig, Chem. Ber. **129** (1996) 227

[3] Recent review on chelate controlled reactions: M. T. Reetz, Acc. Chem. Res. **26** (1993) 462

[4] a) J. Ipaktschi, A. Heydari, Chem. Ber. **126** (1993) 1905; b) H. Waldmann, Angew. Chem. **103** (1991) 1335; c) P. A. Grieco, J. J. Nunes, M. D. Gaul, J. Am. Chem. Soc. **112** (1990) 4595; d) P. A. Grieco, J. D. Clark, C. T. Jogoe, J. Am. Chem. Soc. **113** (1991) 5488; e) J. Ipaktschi, A. Heydari, Angew. Chem. **104** (1992) 335; f) J. Ipaktschi, A. Heydari, Chem. Ber. **125** (1992) 1513; g) K. J. Henry, P. A. Grieco, C. T. Jogoe, Tetrahedron Lett. **33** (1992) 1817; h) P. A. Grieco, R. J. Cooke, K. J. Henry, J. M. VanderRoest, Tetrahedron Lett. **32** (1991) 4665; i) V. G. Saraswathy, S. Sankararaman,J.Org. Chem. **59** (1994) 4665

[5] a) M. T. Reetz, B. Raguse, C. F. Marth, H. M. Hügel, T. Bach, D. N. A. Fox, Tetrahedron **48** (1992) 5731; b) M. T. Reetz, D. N. A. Fox, Tetrahedron Lett. **34** (1993) 1119

[6] a) T. Kunz, H.–U. Reißig, Angew. Chem. **100** (1988) 297; Angew. Chem. Int. Ed. Engl. **27** (1988) 268; b) A. Janowitz, T. Kunz, G. Handke, H.–U. Reißig, Synlett **1989**, 24; H.–U. Reißig, H. Angert, T. Kunz, A. Janowitz, G. Handke, E. Bruce–Adjei, J. Org. Chem. **58** (1993) 6280

[7] Y. Kita, J. Segawa, J.–i. Haruta, H. Yasuda, Y. Tamura, J. Chem. Soc., Perkin Trans.1 **1982**, 1099

[8] a) E. Kunkel, I. Reichelt, H.–U. Reißig, Liebigs Ann. Chem. **1984**, 802; b) T. Kunz, A. Janowitz, H.–U. Reißig, Synthesis **1990**, 43; c) H.–U. Reißig, I. Reichelt, T. Kunz, Org. Synth. **71** (1992) 189

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