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# CONVENIENT FLUORIDE-MEDIATED REACTIONS OF LACTONES WITH SILYL KETENE ACETALS

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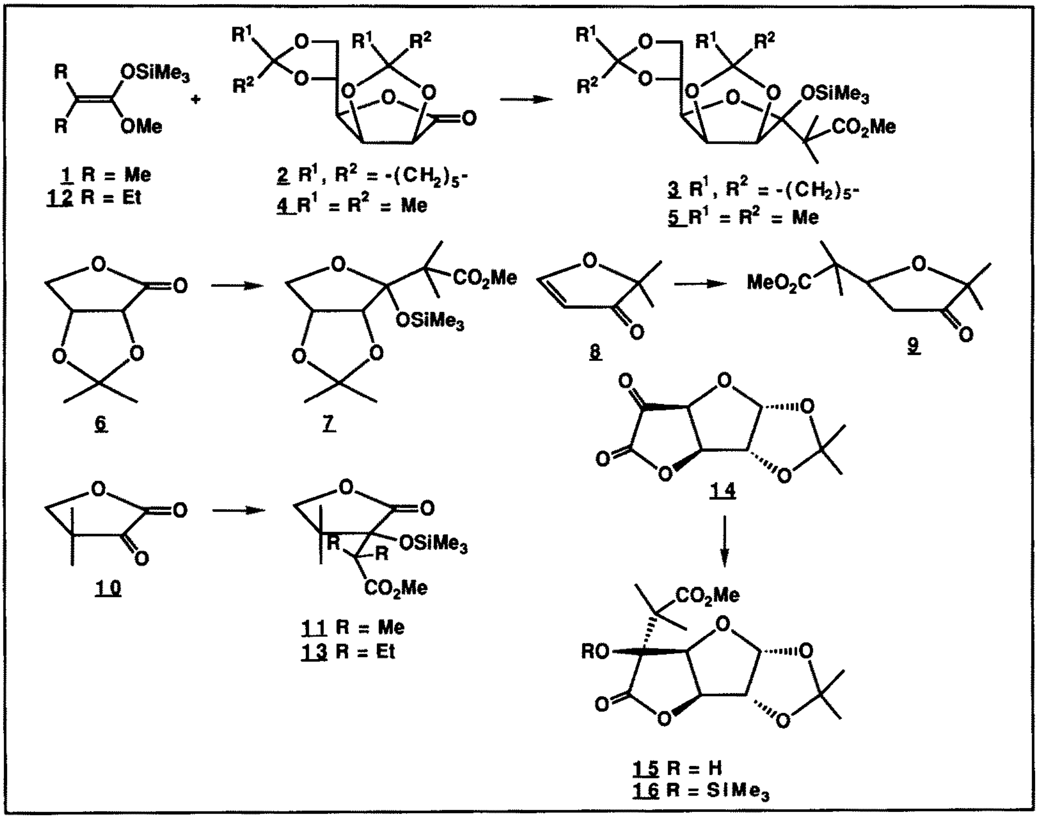
*Key Words:* TASF; aldolisation reactions; silyl ketene acetals; lactones; carbohydrates.

***Abstract:*** *Aldolisation reactions of silyl ketene acetals with lactone carbonyls can be performed under very mild conditions in good yields in the presence of 5-10 mol-% of TASF.*

Silyl ketene acetals have been in the focus of synthetic interest for many years; they are readily available [1-3] and they are well known to add to α,β-unsaturated ketones either in the presence of tris(dimethylamido)sulfonium difluorotrimethylsilicate (TASF) [4] or even without any catalyst in acetonitrile as the solvent [5] to yield the corresponding 1,5-dicarbonyl compounds exclusively. There are numerous examples of their fluoride anion or Lewis-acid catalyzed reactions with aldehydes and ketones [6-10] Michael-acceptors [4, 11] or with organic halides.[12-15] Most recently samarium diiodide [16] has been found as an excellent precursor catalyst for the reactions of silyl ketene acetals with carbonyl compounds but, unfortunately, these reactions are restricted to aromatic aldehydes and ketones or aliphatic aldehydes. Therefore, these reactions are similarly restricted in their applications as do experimental protocols using lanthanide trichloride,[17] $Ln(dppm)_3$ or $Ln(fod)_3$ as a catalyst.[18-21] To the best of our knowledge the reactions of silyl ketene acetals with lactone carbonyls have been obtained only under forced conditions with catalytic amounts of triphenylmethylium hexachloroantimonate [22] or in the presence of a catalyst system consisting of antimony pentachloride, chlorotrimethylsilane, and tin(II) chloride [22]

We wish to report the first successful examples of the very smooth reaction between silyl ketene acetals and lactone carbonyls using tris(dimethylamido)sulfonium difluorotrimethylsilicate, TASF, as the catalyst.

Thus, treatment of the trimethylsilyl ketene acetal of methyl isobutyrate, 1-methoxy-2-methyl-1-trimethylsilyloxypropene (**1**), with 2,3;5,6-di-*O*-cyclohexylidene-D-mannono-1,4-lactone (**2**) in anhydrous THF (2 h, -25°) in the presence of catalytic amounts of TASF yielded chain elongated **3** (74% yield). From the isopropylidene analog **4** under the same conditions **5** (64%) was obtained. 2,3-*O*-Isopropylidene-D-erythronolactone (**6**) which is easily obtained from the degradation of D-isoascorbic acid followed by isopropylidenation [23] afforded **7** ( 3 h, 63% yield).[24, 25]



In a typical procedure, to a solution of the carbonyl compound (2 mmol) in anhydrous THF (2-3 *ml*) and the ketene acetal (4 mmol) a catalytic amount (5-10 mol %) of TASF is added under stirring (under argon). The colour of the reaction mixture turns yellow to orange upon the addition of TASF. After completion of the reaction (as indicated by TLC) the mixture is diluted with ethyl acetate (25 *ml*) and washed with ice water and brine (2 *ml* each). The organic layer is dried over Na$_2$SO$_4$, the solvent is evaporated and the residue is subjected to flash chromatography (silica gel, ethyl acetate/hexanes).[26]

A smooth reaction was observed for the vinylogous lactone 2,2-dimethyl-3(2H)-furanone (**8**) which afforded at 0° within 2 h 88% of the product of the conjugate addition, 2-(5,5-dimethyl-4-oxo-tetrahydrofuran-2-yl)-2-methylpropionic acid methyl ester (**9**).[27–29]

In addition, the mild conditions of this reaction allowed the selective transformation of α-keto lactones at their carbonyl moiety leaving the lactone group unaffected. Thus, dihydro-4,4-dimethyl-2,3-furandione (**10**) reacted with **1** in the presence of TASF at 0° within 1 h to **11** (91%); similarly, **10** gave on reaction with 1-methoxy-2-ethyl-1-trimethylsilyloxy-but-1-ene (**12**) 71% of **13** (10°, 2 h). Even the very sensitive, carbohydrate derived α-keto lactone **14** was transformed within a reaction time of 2 h at 0° in 44% yield stereoselective into 1,2-*O*-isopropylidene-5-*C*-(1,1-dimethyl-methoxycarbonylmethyl)-α-D-glucofuranurono-6,3-lactone (**15**). It should be noted that the silyl ketene acetal reacts only with the ketone function of the keto lactone.[30]

We are currently studying further developments, e.g. stereoselectivity with respect to the newly created stereogenic centres especially for applications in natural product synthesis.

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24 All yields refer to isolated material; all compounds have been fully characterized spectroscopically by IR-, $^{1}$H-NMR, $^{13}$C-NMR, $^{29}$Si-NMR- ($CDCl_3$ as solvent, TMS as internal standard) and MS-spectroscopy; all compounds showed satisfactory elemental analysis (± 0.3%).

25 The obtained configuration at the anomeric centre can be explained by an attack of the reagent from the less hindered face; contrary to reactions of aldonolactones with α-trimethylsilylated esters in the presence of tetra-*n*-butyl-ammonium fluoride (R. Csuk, B. I. Glänzer, *J. Carbohydr. Chem.* **1990**, *9*, 809) no anomerizations took place during these reactions.

26 Selected analytical data: **3**: oil, $[\alpha]^{20}_{D}$ -27.1° (*c* 1.6, $CHCl_3$), $^{1}$H-NMR: 0.16 (*s*, 9 H, $SiMe_3$); 1.23 (*s*, 3 H, Me); 1.31 (*s*, 3 H, Me); 1.47-1.80 (*m*, 20 H, cyclohex.); 3.40 (*s*, 3 H, OMe); 3.95-4.75 (*m*, 6 H); 4.82 (*d*, *J* = 6.2, H-C(4)), $^{29}$Si-NMR. 13.78; **5**: oil, $[\alpha]^{20}_{D}$ -45.16° (*c* 1.5, $CHCl_3$); $^{1}$H-NMR: 0.17 (*s*, 9 H, $SiMe_3$), 1.24, 1.31, 1.38, 1.42, 1.62 (each *s*, 3 H, Me), 3.60-3.62 (*m*, 1 H), 3.67 (*s*, 3 H, OMe), 4.0-4.44 (*m*, 3 H), 4.73 (*dd*, 1 H, *J* = 6, 8), 5.13 (*d*, *J* = 6, 1 H, H-C(4)); $^{29}$Si-NMR: 14.11; **7**: oil, $[\alpha]^{20}_{D}$ +24.4° (*c* 1.9, $CHCl_3$); $^{1}$H-NMR: 0.20 (*s*, 9 H, $SiMe_3$); 1.21, 1.27, 1.38, 1.59 (each *s*, 3 H, Me); 3.66 (*s*, 3 H, OMe); 3.90 (*virt. d*, *J* = 9, 2 H, $H_{A,B}$-C(6)); 4.77 (*m*, 1 H, H-C(5)); $^{29}$Si-NMR: 12.94; **9**: oil; $^{1}$H-NMR: 1.18, 1.22, 1.23, 1.24 (each *s*, 3 H, Me), 2.47 (*bd*, *J* = 9 Hz, 2 H, $CH_2$); 3.68 (*s*, 3 H, OMe); 4.36 (*t*, *J* = 9, CH-O); **11**: oil, $^{1}$H-NMR: 0.20 (*s*, 9 H, $SiMe_3$); 1.07, 1.18, 1.31, 1.47, (each *s*, 3 H, Me); 3.81 and 3.72 (*AB*, *J* = 11.0, 2 H, $CH_2$-O); $^{29}$Si-NMR: 15.14; **13**: oil, $^{1}$H-NMR: 0.16 (*s*, 9 H, $SiMe_3$), 0.71 (*t*, *J* = 7.5, Me), 0.96 (*t*, *J* = 7.6, Me), 1.10 (*s*, 6 H, 2 x Me), 2.68 (*dq*, *J* = 1.2, 7.5, 1 H) and 1.73-2.09 (*m*, 3 H) 3 x $CH_2$, 3.61 (*s*, 3 H, OMe, 3.73 and 3.61 (*AB*, *J* = 8.7, 2 H, $CH_2O$); $^{29}$Si-NMR: 14.99; **15**: mp. 98-99°, $[\alpha]^{20}_{D}$ +12.86° (*c* 1.4, $CHCl_3$), $^{1}$H-NMR: 1.37 (*s*, 6 H) 1.45 (*s*, 3 H), 1.53 (*s*, 3 H) 4 x Me, 3.66 (*bs*, 1 H, exch. with $D_2O$), 3.73 (*s*, 3 H, OMe), 4.82 (*d*, *J* = 4.3, 1 H, H-C(3)); 4.85 (*d*, *J* = 3.5, 1 H, H-C(2)); 4.92 (*d*, *J* = 4.3, 1 H, H-C(4)); 5.89 (*d*, *J* = 3.5, 1 H, H-C(1)); only traces of the 5-*O*-trimethylsilyl derivative **16** could be detected; it can be obtained, however, by reaction of **15** with **1** with TASF in high yield.

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