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STEREOCHEMICAL CONSEQUENCE IN THE ELIMINATION OF β-HYDROXYALKYLSILANES: STEREOSELECTIVE FORMATION OF (*Z*)- AND (*E*)-ALKYLIDENE-γ-BUTYROLACTONES

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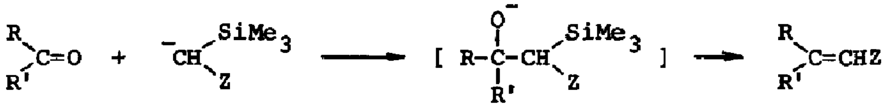
Summary: Titanium(IV) chloride-mediated reaction of 4,5-dihydro-2-(trimethylsiloxy)-3-(trimethylsilyl)furan (1a) with acetaldehyde gave diastereomerically pure (3*S**, 1'*R**)-4,5-dihydro-3-(1'hydroxyethyl)-3-(trimethylsilyl)-2(3H)furanone (2a), which afforded selectively either (*Z*)- or (*E*)-α-ethylidene-γ-butyrolactone (3a) under proper conditions. Facile isomerization of 2a into diastereomerically pure (3*S**, 1'*R**)-4,5-dihydro-3-{1'-(trimethylsiloxy)ethyl}-2(3H)furanone (4) suggests an intriguing stereochemical outcome from 2a to (*E*)-3a *via* an enolate of 4.

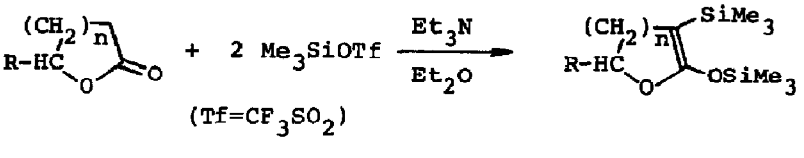
It has been well precedented that the addition of an α-silyl carbanion stabilized by an electron-withdrawing group(Z) to an aldehyde or ketone forms a presumed β-oxidoalkylsilane, which undergoes spontaneous elimination even at low temperature to give an olefinic compound usually as a mixture of geometrical isomers (eq. 1).[1)]



(1)

In contrast, it is noted that the reaction of aldehydes with an enolate generated from α-(trimethylsilyl)-γ-butyrolactone reportedly gives an α-alkylidene γ-butyrolactone with predominant (*E*)-geometry,[2)] the results implicating stereospecific elimination of a sole intermediate β-oxidosilane rather than thermodynamically preferred formation of the trans olefin. However, few preparations of diastereomerically pure β-hydroxyalkylsilanes have been reported in the literature

We wish to report here a preparation of one diastereomer of a β-hydroxyalkylsilane derived from γ-butyrolactone and the stereochemical consequence in the elimination of the diastereomer under proper conditions. Thus 4,5-dihydro-2-(trimethylsiloxy)-3-(trimethylsilyl)furan (1a) was prepared from γ-butyrolactone by a literature method (eq. 2)[4)]



1a; n=1, R=H
1b; n=1, R=Me
1c; n=2, R=H

(2)

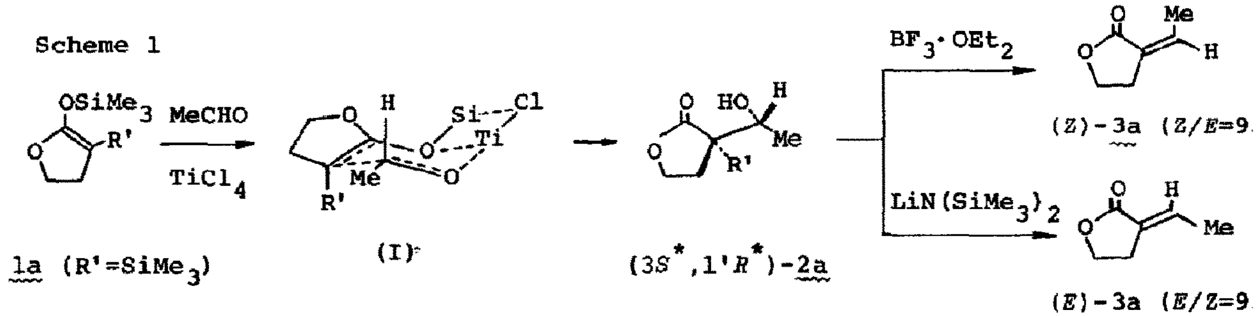
Similarly, 1b and 1c were prepared in good yields from γ-valerolactone and δ-valerolactone, respectively.

$TiCl_4$-assisted aldol reaction was carried out in the following procedure: To a cooled (-78°C) and stirred solution of acetaldehyde (1.7 ml, 30 mmol) and $TiCl_4$ (1.7 ml, 15 mmol) in dry dichloromethane (6 ml) was added dropwise 1a (3. g, 15 mmol) dissolved in dichloromethane (12 ml) over a period of 0.5 h. The r tion mixture was stirred for additional 1.5 h and quenched with methanol (15 ml Aqueous workup followed by usual purification gave analytically pure 4,5-dihydr 3-(1'-hydroxyethyl)-3-(trimethylsilyl)-2(3H)furanone (2a) as a white solid (2.9 98% yield). NMR ($CDCl_3$, TMS): δ 0.19 (s, 9H), 1.23 (d, *J* = 6.2 Hz, 3H), 2.15-2.75 (m, 2H), 2.87 (brs, 1H), and 3.92-4.53 ppm (m, 3H). IR (CCl_4 soln): 3620 (OH free), 3480 (OH hydrogen bonded), 1735 (C=O), 1450 and 1250 cm^{-1} ($SiMe_3$).

The most striking is that 2a was readily obtained as a pure diastereomer.[5] In fact, in another run at a higher reaction temperature (-40°C) there obtained mixture of diastereomers (ratio 85 : 15) which are evidenced by NMR using Eu(fo Doublets of methyl protons were observed at δ 1.23 and 1.36 ppm, respectively.

Diastereomerically pure 2a thus obtained is most likely (3*S**, 1'*R**) on the basis of a preferred six-membered transition state of directed aldol reactions which are of current interest,[6] and of results of the Peterson olefination rea tions as discussed below. The stereochemical correlations obtained in the pres study are outlined in Scheme 1.

Scheme 1



1a (R'=$SiMe_3$)

(I)

(3*S**,1'*R**)-2a

(*Z*)-3a (*Z*/*E*=9

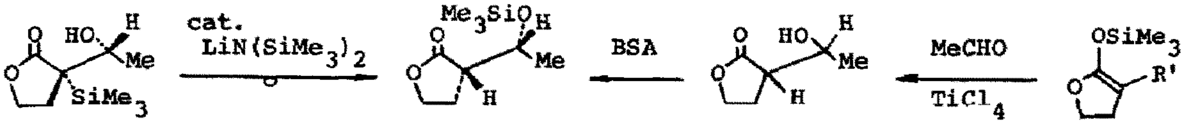
(*E*)-3a (*E*/*Z*=9

Treatment of 2a (0.202 g, 1.0 mmol) with $BF_3 \cdot OEt_2$ (1.26 ml, 10 mmol) in dichlor methane (10 ml) at -20°C for 2.5 h followed by usual work-up afforded quantitatively α-ethylidene-γ-butyrolactone (3a) with predominant (*Z*)-configuration,[7] ratio *Z*/*E* being 95/5 by GLC analysis. Since it is known that the acid-catalyze elimination of β-hydroxyalkylsilanes takes place by an anti pathway,[3] highly stereoselective formation of (*Z*)-3a reinforces the relative configuration of diastereomerically pure 2a to be (3*S**, 1'*R**).

Reaction of 2a (1.0 mmol) with lithium bis(trimethylsilyl)amide, prepared from hexamethyldisilazane (0.30 ml, 1.4 mmol) and BuLi (1.2 mmol), in dry THF (ml) at -78°C for 2.5 h yielded (*E*)-3a[8] (58%), which was contaminated with 4% o (*Z*)-3a, α-vinyl-γ-butyrolactone (17%), and 4,5-dihydro-3-{1'(trimethylsiloxy)-ethyl}-2(3H)furanone (4) (19% area ratio by GLC), which was found to diminish w prolonged reaction time.

Formation of 4 must arise from facile 1,3-migration of a trimethylsilyl group from carbon to oxygen. That 4 unexpectedly consisted of one diastereomer was firmly verified in the following way as depicted in scheme 2.

Scheme 2



(3*S**,1'*R**)-2a (3*S**,1'*R**)-4 5 (diastereomers) 1a (R'=H)

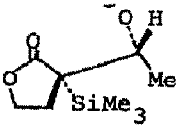
Preparation of 4,5-dihydro-3-(1'-hydroxyethyl)-2(3H)furanone (5) was carried out exactly in the same manner as that of 2a using 4,5-dihydro-2-(trimethylsiloxy)furan (1a, R'=H) (0.55 g, 3.5 mmol). Purified 5 (56% yield) was obtained as a mixture of diastereomers in a ratio 70/30.[9)] On the basis of preferred transition state (I) (R'=H) in the scheme 1, these diastereomers may well be assigned as (*R**,*R**) and (*R**,*S**), respectively.

Silylation of the alcohol (5) (0.137 g, 0.5 mmol) with bis(trimethylsilyl)-acetamide (0.25 ml, 1.2 mmol) in dry acetonitrile (10 ml) gave, after column-chromatographic purification, a diastereomeric mixture of 4 (0.083 g, 39%), which are analyzed by GLC and by NMR using $Eu(fod)_3$.[9)]

Finally, a THF solution of 2a (0.187 g, 0.92 mmol) was treated with a catalytic amount of $LiN(SiMe_3)_2$ (5 mol%) at -78°C for 3 h. Usual workup and separation of crude products by a short column afforded (*E*)-3a (0.028 g, 27%) and diastereomerically pure 4 (0.124 g, 66%), respectively. Unambiguous assignment of (3*S**, 1'*R**)-4 could be made by GLC and NMR analyses in comparison with the above sample.

The significant features of the present base-induced isomerization and β-elimination of 2a to give 4 and (*E*)-3a, respectively, may be twofold.

First, it is clearly indicated that under base-catalyzed conditions the β-oxidosilane (II) once formed from 2a may undergo either syn-elimination to give (*E*)-3a or migration of a trimethylsilyl group to form a lactone enolate (III), which, in turn, is protonated with 2a present in excess to give stereoselectively (3*S**, 1'*R**)-4 and the β-oxidosilane (II). Although the stereoselective protonation may be very specific in steric origin in the present reaction, it is important to find that the 1,3-migration of a trimethylsilyl group in (II) to form an ambident anion (III) is faster than a direct syn-elimination to give (*E*)-3a.



(II)

(III)

Rapid 1,4-migration of a trimethylsilyl group in γ-oxidoalkylsilanes[8)] as well 1,2-migration in α-oxidoalkylsilanes[10)] has already been discussed.

Secondly and consequently, all data presented here let us suggest that in base-induced elimination of β-hydroxyalkylsilanes (and intermediate β-oxidosila also) where a carbanion-stabilizing group is located on a carbon α to the silic facile 1,3-migration of a silyl group very likely takes part in the eliminatio pathway, the resulting β-siloxyalkyl carbanion entering the final elimination s to give product olefins. Although this pathway does not necessarily preclude a direct syn-elimination as mentioned above, stereoselective formation of (*E*)-**3a** from **2a** is alternatively accounted for by an exclusive anti-elimination of a trimethylsiloxy group form (III), which is consonant with the fact that (III) i found to be protonated with inversion of configuration at carbon.

Different stereochemical outcome from **1b** and **1c** will be reported in due co

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5) Similarly, the reaction of **1a** with benzaldehyde gave a diastereomerically p β-hydroxyalkylsilane which afforded on treatment with $BF_3\cdot OEt_2$ almost pure (*Z*)-α-benzylidene-γ-butyrolactone.[7)] NMR ($CDCl_3$, TMS) δ 3.07 (dt, *J* = 7.2, 2.4 Hz, 2H), 4.35 (t, *J* = 7.2 Hz, 2H), 6.97 (t, *J* = 2.4 Hz, 1H), 7.20-7.55 3H), and 7.68-7.95 ppm (m, 2H).
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