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[3,3]-SIGMATROPIC REARRANGEMENT OF SILYL KETENE ACETALS OF METHYL α-(ALLYLOXY)ACETATES.[1]

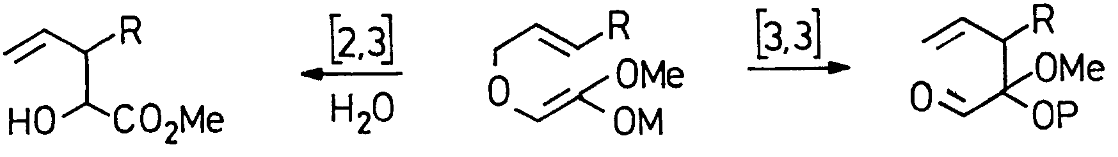
Stanley Raucher*[2] and Linda M. Gustavson

Department of Chemistry, University of Washington, Seattle, Washington 98195

Abstract: Although the lithium enolate 2a undergoes [2,3]-sigmatropic rearrangement to give 4a, the silyl ketene acetals 3 undergo [3,3]-sigmatropic rearrangement to give 5. This is the first reported [3,3]-sigmatropic rearrangement of a 1,1-dioxy-3-oxa-1,5-diene.

Sigmatropic rearrangements provide versatile means for the formation of new carbon-carbon bonds with the control of both stereochemistry and regiochemistry, and they have been utilized for the synthesis of a wide variety of natural products.[3] The [3,3]-sigmatropic rearrangement of silyl ketene acetals derived from allyl esters by the Ireland procedure[4] has proven to be especially useful. The [2,3]-sigmatropic (Wittig) rearrangement of α-(allyloxy)acetic acid dianions has also been reported recently.[5]

The 1,1-dioxy-3-oxa-1,5-dienes 2 or 3 provide a rather unusual system which could undergo either [2,3]-sigmatropic rearrangement to give 4, or [3,3]-sigmatropic rearrangement to give 5. Although the effect of substituents on sigmatropic rearrangements has been examined for a variety of systems, to date there have been only limited reports involving the sigmatropic rearrangements of 1-oxy-3-oxa-1,5-dienes.[6,7,8] We now wish to report the results of studies involving the sigmatropic rearrangements of 1,1-dioxy-3-oxa-1,5-dienes 2 and 3.



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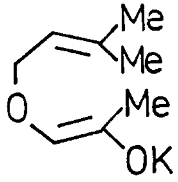
2 M = Li
3 M = $SiMe_2t$-Bu

5 P = $SiMe_2t$-Bu

When methyl α-(geranyloxy)acetate (1a) was treated with LDA at -78 °C, warmed to 0 °C and quenched with H_2O, the [2,3]-sigmatropic rearrangement product 4a was obtained in 63% yield.[9] This result is analogous to that obtained by Nakai[5] for the rearrangement of the dianion of α-(geranyloxy)acetic acid. In marked contrast, when 1a was treated with LDA and trapped with $t\text{-BuMe}_2\text{SiCl}$ under carefully controlled conditions, the silyl ketene acetal 3a was obtained with no evidence of [2,3]-sigmatropic rearrangement.[10] Thermolysis of a solution of 3a in toluene at 110 °C for 2 hours provided the [3,3]-sigmatropic rearrangement product 5a in 65% yield. Results for the [3,3]-sigmatropic rearrangement of a variety of silyl ketene acetals 3 prepared from methyl α-(allyloxy)acetates 1 are summarized in Table I. This method allows the conversion of allylic alcohols to protected α-keto aldehydes with control of regiochemistry (cf. entries b and c, d and e). The [3,3]-sigmatropic rearrangement of methyl α-(allyloxy)-propionates to selectively protected α-diketones has also been effected (entries i and j).

The results for the rearrangements of these 1,1-dioxy-3-oxa-1,5-dienes are similar to those reported for 1-oxy-3-oxa-1,5-dienes by Thomas[6] and Solomon[7], but differ from those of Koreeda.[8] Thomas[6] observed only [2,3]-sigmatropic rearrangement product from the potassium enolate 6, whereas Solomon[7] obtained only [3,3]-sigmatropic rearrangement products from the enol silyl ethers 7. In contrast, Koreeda[8] observed only [3,3]-sigmatropic rearrangement product from 8 (M = K, Na, or Me_3Si), with the fastest rearrangement rate for M = K, but 20% of [2,3]-sigmatropic rearrangement product from 8 (M = Li). Although an explanation for these differences in behavior is not obvious, a subtle balance of factors appears to be in effect.



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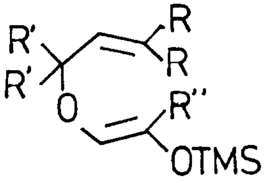
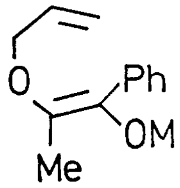


7 R = H, R' = H, R" = Ph
R = Me, R' = H, R" = Me or Ph
R = H, R' = Me, R" = Ph



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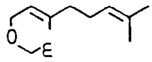
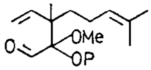
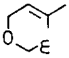
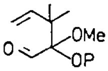
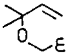
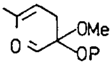
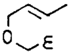
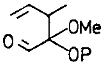
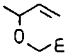
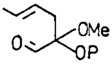
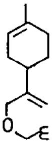
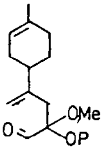
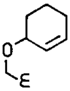
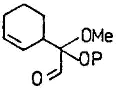
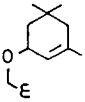
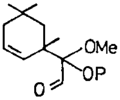
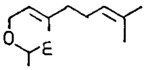
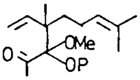
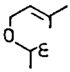
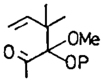
General Procedure. To $i\text{-Pr}_2\text{NH}$ (23 mg, 0.23 mmol) in THF (0.2 mL) under Ar at 0 °C was added 2.6M n-BuLi in hexane (0.09 mL, 0.23 mmol). The solution was cooled to -78 °C, and a solution of 1a (37 mg, 0.16 mmol) in THF (0.4 mL) was added. The reaction was stirred for 25 min at -78 °C, and HMPA (80 μL) was added. A solution of $t\text{-BuMe}_2\text{SiCl}$ (35 mg, 0.23 mmol) in THF (0.4 mL) was then added. The reaction was stirred for 1 hour at -78 °C, 1 hour at -40 °C, 1 hour at 0 °C, and 1 hour at 25 °C. The reaction was quenched with 0.1M NaOH and extracted with pentane. The pentane extracts were washed with 0.1M NaOH, dried (K_2CO_3) and evaporated to give the 3a (40 mg). A solution of 3a in toluene (7 mL) was heated under Ar at 110 °C for 2 hours. The toluene was evaporated, and the residue was purified by flash chromatography (10% EtOAc-hexane) to give 5a as colorless liquid (35 mg, 0.10 mmol, 65% yield).[11]

TABLE I

Entry	α-Allyloxy Ester 1	Rearrangement Product 5	Yield
a			65%
b			65%
c			35%
d			60%
e			51%
f			71%
g			65%
h			50%
i			66%
j			52%
	E = CO_2Me	P = $SiMe_2t$-Bu	

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(9) Starting material 1a was obtained if the reaction was quenched at -78 °C.

(10) If the trapping is not carried out as detailed in the sample experimental procedure, some [2,3]-sigmatropic rearrangement occurs.

(11) The methyl α-(allyoxy)acetates 1a-1h were prepared by reaction of allylic alcohols with NaH (10 equiv) and $ClCH_2CO_2H$ (2.5 equiv) in THF containing EtOH (0.05 equiv), followed by CH_2N_2 treatment. The methyl α-(allyoxy)propionates 1i and 1j were prepared by alkylation of 2a and 2b with MeI. For compounds 5 which contain two chiral centers, mixtures of diastereomers (ca. 9:1) were obtained. Yields refer to isolated, chromatographically pure products. All new compounds gave spectroscopic data in accord with the proposed structures. ^{1}H NMR data ($CDCl_3$): 5a (500 MHz) δ: 0.2 (d, J = 6, 6H), 0.9 (s, 9H), 1.1 (s, 3H), 1.55 (s, 3H), 1.78 (s, 3H), 1.75-1.88 (m, 4H), 3.21 (s, 3H), 5.00 (d, J = 18, 1H), 5.05 (dd, J = 8, 6, 1H), 5.15 (d, J = 11, 1H), 5.85 (dd, J = 18, 11, 1H), 9.55 (s, 1H). 5b (60 MHz) δ: 0.2 (s, 6H), 0.9 (s, 9H), 1.0 (s, 6H), 2.1 (s, 3H), 3.15 (s, 3H), 4.90 (d, J = 18, 1H), 5.0 (d, J = 10, 1H), 6.0-6.5 (m, 1H). 5c (60 MHz) δ: 0.2 (s, 6H), 0.9 (s, 9H), 1.6 (s, 3H), 1.7 (s, 3H), 2.4 (s, 1H), 2.5 (s, 1H), 3.3 (s, 3H), 5.1 (dd, J = 8, 6, 1H), 9.5 (s, 1H). 5d (60 MHz) δ: 0.2 (s, 6H), 1.0 (s, 9H), 1.3 (d, J = 8, 3H), 2.9 (m, 1H), 3.3 (s, 3H), 4.9-5.6 (m, 2H), 5.6-6.1 (m, 1H), 9.4 (s, 1H). 5e (500 MHz) δ: 0.13 (s, 6H), 0.90 (s, 9H), 1.66 (d, J = 3, 3H), 2.50-2.56 (m, 2H), 3.20 (s, 3H), 5.28-5.37 (m, 1H), 5.45-5.56 (m, 1H) 9.5 (s, 1H); Irradiation at δ 1.67 collapsed m at 5.45-5.56 to d with J = 15. 5f (60 MHz) δ: 0.2 (s, 6H), 0.9 (s, 9H), 1.7-2.2 (m, 10H), 2.5-2.7 (s, 2H), 3.3 (s, 3H), 4.8-5.0 (s, 2H), 5.4-5.6 (s, 1H), 9.6 (s, 1H). 5g (80 MHz) δ: 0.2 (s, 6H), 1.1 (s, 9H), 1.15-2.00 (m, 7H), 3.30 (s, 3H), 5.9 (s, 2H), 9.75 (s, 1H). 5h (60 MHz) δ: 0.2 (d, J = 4, 6H), 0.9-1.2 (m, 18H), 1.4-1.6 (m, 4H), 3.20 (s, 3H), 5.4-5.7 (m, 2H), 9.4 (s, 0.1H) and 9.5 (s, 0.9H), diastereomeric CHO. 5i (60 MHz) δ: 0.2 (m, 6H), 0.9-1.2 (m, 12H), 1.2-1.4 (m, 2H), 1.6-1.8 (m, 8H), 2.10-2.15 (m, 3H), 3.15, 3.20 (m, 3H), 4.7-5.3 (m, 3H), 5.6-6.2 (m, 1H). 5j (60 MHz) δ: 0.2 (s, 6H), 0.9 (s, 9H), 1.0 (s, 6H), 2.1 (s, 3H), 3.15 (s, 3H), 4.90 (d, J = 18, 1H), 5.0 (d, J = 1.0, 1H), 6.0-6.5 (m, 1H).

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