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Stereoselective Synthesis of (2E,4E)- and (2Z,4E)-2,4-Alkadienoates by the Ester Enolate Claisen Rearrangement of (E)-1-Alkyl-3-trimethylsilyl-2-propenyl Glycolates Followed by the Peterson Reaction

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The ester enolate Claisen rearrangement of (E)-1-alkyl-3-trimethylsilyl-2-propenyl glycolates gave (E)-*erythro*-2-hydroxy-3-trimethylsilyl-4-alkenoates with high diastereoselectivity, which were stereoselectively converted into (2E,4E)- and (2Z,4E)-2,4-alkadienoates by the Peterson reaction.

(2E,4E)- and (2Z,4E)-Alkadienoates are valuable synthetic intermediates for naturally occuring compounds such as insecticide,[1,2] insect pheromone,[3] and other biologically active compounds.[4] There have appeared a number of synthetic methods for (2E,4E)-alkadienoates,[2,5] but little is known for (2Z,4E)-alkadienoates.[6] Recently we have demonstrated that the ester enolate Claisen rearrangement of allyl glycolates exhibits an extremely high degree of diastereoselectivity to afford 2-hydroxy-3-alkyl-4-alkenoic acids;[7] *i.e.*, the use of the allylic ester with (E)- or (Z)-geometry gives the *erythro*- or *threo*-acid, respectively, with 98% of diastereoselectivity. In this letter, we wish to report that the analogous Claisen rearrangement of (E)-1-alkyl-3-trimethylsilyl-2-propenyl glycolates (**1**) is also feasible, and the rearranged products, methyl (E)-*threo*-2-hydroxy-3-trimethylsilyl-4-alkenoates (**2**) undergo stereospecific *syn* or *anti* β-elimination reaction of β-hydroxysilane under basic or acidic conditions, (the Peterson reaction)[8] to afford (2E,4E)- and (2Z,4E)-2,4-alkadienoates, respectively.

Esters **1** (R = CH_3, n-C_3H_7, n-C_5H_{11}) were prepared from 2-methyl-1,3-dioxolane-4-one and (E)-1-trimethylsilyl-1-alken-3-ols in 31 - 51% yields[9] (conversion yields, 69 - 82%), which were obtained by reduction of 1-trimethylsilyl-1-alkyn-3-ols with

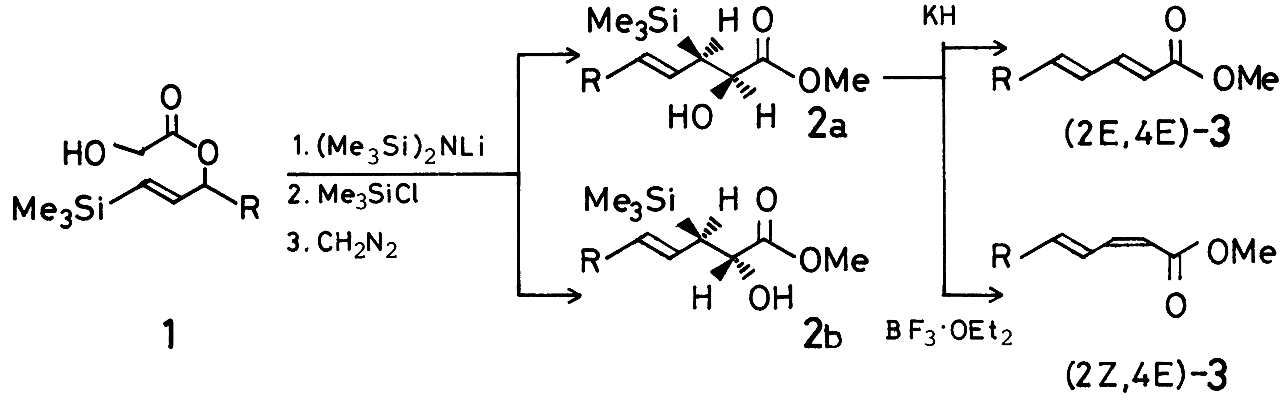


Table 1. The Ester Enolate Claisen Rearrangement of Ester 1

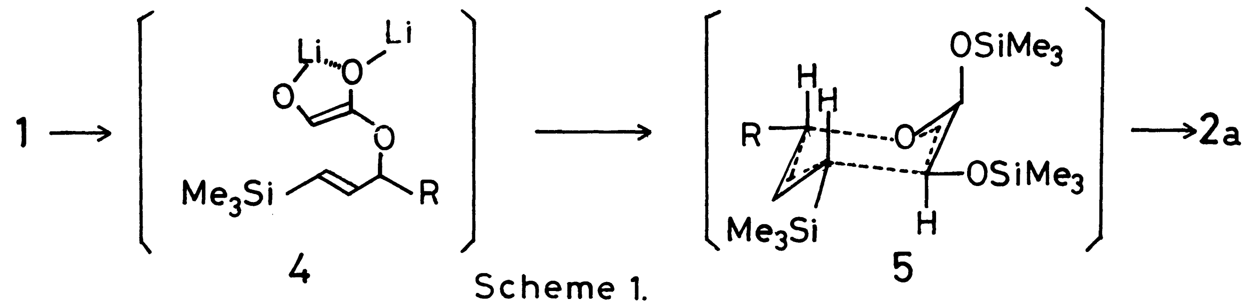
R	Yield of 2/%	Ratio of 2a : 2b[a)]
CH_3	93	97 : 3 (100 : 0)[b)]
n-C_3H_7	85	94 : 6 (100 : 0)
n-C_5H_{11}	89	94 : 6 (100 : 0)

a) The ratio was determined by GLC using capillary column (SE-30 50m).

b) Corrected values based on the E/Z ratio of 1-trimethylsilyl-1-alken-3-ol.

$NaAlH_2(OCH_2CH_2OCH_3)_2$ in 82% yield with E/Z ratio of 94/6 - 97/3.[10)] Ester 1 was submitted to the treatment with lithium hexamethyldisilazide (3 equiv.) in THF at -78 °C for 2 h, then chlorotrimethylsilane (3 equiv.) was added to the mixture as a trapping reagent of the dianion of the enolate formed. The mixture was allowed to warm up to room temperature over 1 h and stirred for additional 2 h. After aqueous workup, 2 was isolated in high yield as the corresponding methyl ester by the treatment of the rearranged product with diazomethane. The *threo*- and *erythro*-isomers (2a and 2b) were easily separated by silica-gel TLC. The results are listed in Table 1. GLC and ^{1}H NMR[11)] analysis of ester 2 showed predominant formation of *threo*-isomer 2a, which can be comfirmed by the coupling constant of the α and β vicinal protons, J = 5.5 Hz for the major isomer 2a and J = 2.0 - 2.4 Hz for the minor isomer 2b.[12)] The *erythro*- and *threo*-stereochemistry is also established by the Peterson reaction (*vide infra*). Considering the E/Z ratio of the starting material 1, the complete diastereoselectivity of the Claisen rearrangement was achieved. The high diastereoselectivity is reasonably explained by the transition state 5, which is formed by trapping the enolate dianion 4 with chlorotrimethylsilane. The geometry of 4 produced from α-hydroxy ester 1 is controlled by intramolecular five-membered chelate structure.[13)] The chairlike transition state with the bulky trimethylsilyl group and the substituent R at equatorial positions give 2a with high *threo*-diastereoselectivity and (E)-stereoselectivity (Scheme 1).

Next, the Peterson reaction[8)] of 2a, utilizing the 2-hydroxy and 3-trimethylsilyl groups, was examined to synthesize stereoselectively (2E,4E)- and (2Z,4E)-2,4-alkadienoates. Treatment of *threo*-ester 2a with potassium hydride (1 equiv.) in THF at -78 °C - -40 °C gave methyl (2E,4E)-2,4-alkadienoates (3) with 99% stereoselectivity including (2E,4E)-isomers (1%) in high yields. On the other hand, treatment of 2a with boron trifluoride etherate (12 equiv.) in dichloromethane at -20 °C for 22 - 50 h afforded methyl (2Z,4E)-2,4-alkadienoates with more than 90% stereoselectivity along with (2E,4E)-isomers (3 - 5%) and (2Z,4Z)-isomers (2 - 7%), and



Scheme 1.

Table 2. The Peterson Reaction of Ester 2a

Reagent	R	Yield of 3/%	Ratio[a]			
			2E,4E	2E,4Z	2Z,4E	2Z,4Z
KH	CH_3	89	99	1	0	0
	$n\text{-}C_3H_7$	98	99	1	0	0
	$n\text{-}C_5H_{11}$	100	99	1	0	0
$BF_3 \cdot OEt_2$	CH_3	65	3	0	90	7
	$n\text{-}C_3H_7$	74	5	0	93	2
	$n\text{-}C_5H_{11}$	71	4	0	91	5

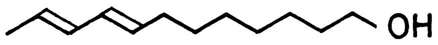
a) The ratio was determined by GLC (capillary column SE-30, 50 m) comparing with authentic samples.

(2E,4E)-isomers were easily separable from the isomeric mixture by silica-gel TLC. These results are shown in Table 2.

For an example of the synthetic utility of the present method, the stereocontrolled synthesis of (8E,10E)- and (8Z,10E)-8,10-dodecadienol was carried out. The former (6) is the sex pheromone of the codling moth (*Laspeyresia pomonella*),[3,14] and the latter (7) is the sex attractant of *Hedya ochroleucana*.[15,16]

Reduction of methyl (2E,4E)-2,4-hexadienoate (3, R = Me) with $LiAlH_4$ followed by treatment with acetic anhydride gave (2E,4E)-2,4-hexadienyl acetate (8) in 62% yield with 99% purity. Coupling of the Grignard reagent (9) with ester 8 in the presence of a catalytic amount of CuI[17] gave (8E,10E)-8,10-dodecadienol (6) in 67% yield with 98% geometrical purity after removal of the protecting group. On the other hand, (2Z,4E)-2,4-hexadienyl acetate (10) obtained in 68% yield with 92% purity from methyl (2Z,4E)-2,4-hexadienoate (3, R = Me) in a similar manner as above was coupled with Grignard reagent (11) to give (8E,10Z)-8,10-dodecadienol (7) in 23% yield with 85% purity.

Thus, the chelation-controlled ester enolate Claisen rearrangement of (E)-1-alkyl-3-trimethylsilyl-2-propenyl glycolates provided (E)-*threo*-2-hydroxy-3-trimethylsilyl-4-alkenoates, which were stereoselectively converted into (2E,4E)- and (2Z,4E)-2,4-alkadienoates of useful precursors for the synthesis of insect pheromone and insecticide.



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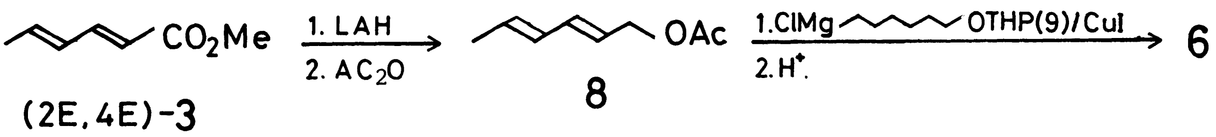

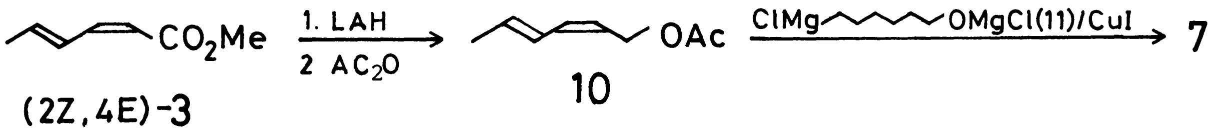

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11) ^{1}H NMR (CCl$_4$), 2a(R = Me): δ 0.00 (9H, S), 1.73 (3H, d, J = 5 Hz), 1.90 - 2.13 (1H, m), 2.72 (1H, d, J = 6 Hz), 3.71 (3H, S), 4.18 (1H, dd, J = 5.5 Hz, J = 6 Hz), 5.26 - 5.50 (2H, m). 2b(R = Me): δ 0.06 (9H, S), 1.68 (3H, d, J = 5 Hz), 1.95 - 2.15 (1H, m), 2.80 (1H, d, J = 5 Hz), 3.20 (3H, S), 4.28 (1H, dd, J = 2.4 Hz, J = 5 Hz), 5.38 - 5.56 (2H, m). 2a(R = n-C$_3$H$_7$): δ 0.00 (9H, S), 0.92 (3H, t, J = 6 Hz, 1.10 - 1.73 (2H, m), 1.80 - 2.22 (3H, m), 2.73 (1H, d, J = 6 Hz), 3.71 (3H, S), 4.15 (1H, dd, J = 5.5 Hz, J = 6 Hz), 5.21 - 5.43 (2H, m). 2b(R = n-C$_3$H$_7$): δ 0.02 (9H, S), 0.83 (3H, t, J = 6 Hz), 1.00 - 1.60 (2H, m), 1.60 - 2.16 (3H, m), 2.68 (1H, d, J = 5 Hz), 3.63 (3H, S), 4.21 (1H, dd, J = 2.2 Hz, J = 5 Hz), 5.13 - 5.40 (2H, m). 2a(R = n-C$_5$H$_{11}$): δ 0.00 (9H, S), 0.88 (3H, t, J = 7 Hz), 1.30 - 1.50 (6H, m), 1.73 - 2.15 (3H, m), 2.65 (1H, d, J = 6 Hz), 3.68 (3H, S), 4.13 (1H, dd, J = 5.5 Hz, J = 6 Hz), 5.20 - 5.42 (m, 2H). 2b(R = n-C$_5$H$_{11}$): δ 0.02 (9H, S), 0.82 (3H, t, J = 5 Hz), 1.03 - 1.58 (6H, m), 1.59 - 2.10 (3H, m), 2.38 - 2.80 (1H, br S), 3.60 (3H, S), 4.18 (1H, d, J = 2 Hz), 5.10 - 5.36 (2H, m).

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