CHEMISTRY LETTERS, pp. 1457-1458, 1985.

DIASTEREOSELECTIVE SYNTHESIS OF 2-HYDROXY-3,4-ALKADIENOIC ACIDS BY THE ESTER ENOLATE CLAISEN REARRANGEMENT OF PROPARGYL GLYCOLATES

Tamotsu FUJISAWA,* Eisaku MAEHATA, Hiromasa KOHAMA, and Toshio SATO
Chemistry Department of Resources, Mie University, Tsu, Mie 514

The ester enolate Claisen rearrangement of propargyl glycolates gave 2-hydroxy-3,4-alkadienoic acids with high diastereoselectivity, which was confirmed by stereospecific transformation of the acids into dihydrofuranmethanols.

Allenes with α- or β-oxygen functionality are very useful precursors for the synthesis of valuable compounds, such as furanones,[1] γ-[2] and δ-lactones,[3] dihydrofurans,[4] and dihydropyrans.[5] Therefore diastereoselective synthesis of allenes has been worthy of remark for their usefulness. We now wish to report here the diastereoselective synthesis of 2-hydroxy-3,4-alkadienoic acids by the ester enolate Claisen rearrangement of propargyl glycolates (1).[6]

Ester 1 prepared by the reaction of the lithium salts of propargylic alcohols with 2-methyl-1,3-dioxolane-4-one was treated with lithium hexamethyldisilazide (3 equiv.) in THF at -78 °C for 2 h. After adding chlorotrimethylsilane (3 equiv.) as a trapping reagent of the dianion of the enolate formed, the reaction mixture was allowed to warm up to room temperature over 6 h and stirred for 2 h. After an extractive workup, 2-hydroxy-3,4-alkadienoic acid was simply isolated by distillation. In the present reaction, lithium hexamethyldisilazide and THF are suitable as a base and a solvent, respectively. Lithium diisopropylamide and 2,2,6,6-tetramethylpiperidide gave no desired product and the use of ether or dimethoxyethane resulted in the decrease of both yield and diastereoselectivity. The result of the ester enolate Claisen rearrangement of 1 is summarized in Table 1. It is noteworthy that the diastereoselectivity in the rearrangement is more than 92%.

The configuration of 2-hydroxy-3,4-alkadienoic acids (3) was determined by conversion of 3 to dihydrofuranmethanols (5). The cyclization of 3 (R^1 = Me, R^2 = Me_3Si) with $AgBF_4$ (1 equiv.) in $CHCl_3$ at room temperature for 3 d gave the dihydrofuran 4,[7] which was reduced without purification with $LiAlH_4$ in ether at -20 °C for 2 h to give dihydrofuranmethanols 5 in 35% yield from 3. NMR analysis using

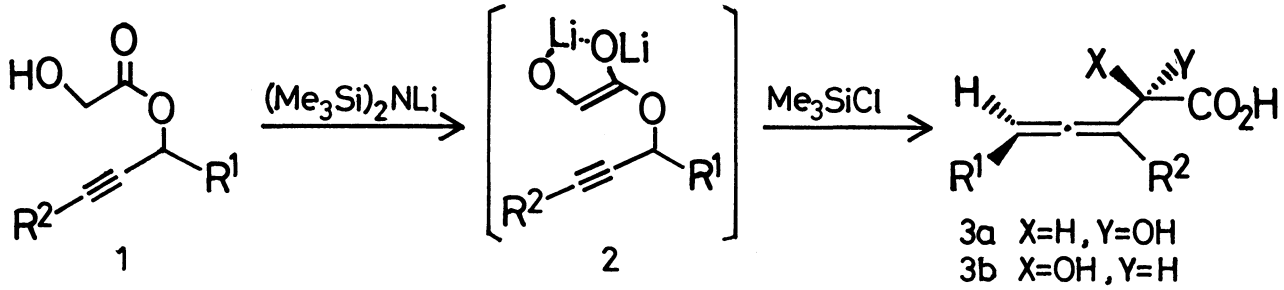
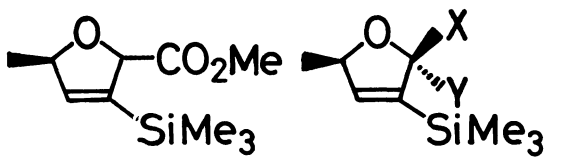


Table 1. The Ester Enolate Claisen Rearrangement of Ester 1[a)]

R^1	R^2	Yield of 3/%[b)]	3a : 3b[c)]
H	Me	71	-
H	Me_3Si	47[d)]	-
Me	Me	72	92 : 8
Me	Me_3Si	88	95 : 5
Me	n-Bu	59	94 : 6
Et	Me_3Si	69	94 : 6
n-Pr	Me_3Si	54	94 : 6

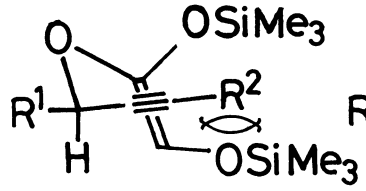
a) All products gave satisfactory NMR and IR spectra. b) Isolated yield by distillation. c) The ratio was determined by GLC using a capillary column, FFAP 50 m on the corresponding methyl ester of 3. d) The starting material was recovered in 27% yield.

the shift reagent, $Eu(fod)_3$ indicated that the major product 5a is the trans isomer, and GLC analysis of 5 showed that the isomer ratio of 5a : 5b is 95 : 5 which accords with that of 3. An authentic 76 : 24 mixture of 3 (R^1 = Me, R^2 = Me_3Si) was converted in the same manner into 5 in a ratio of 76 : 24.[8)] This result indicates that the conversion of 3 to 5 is stereospecific.[9)] Accordingly the structure of the major diastereomer of the rearranged product of 1 is assigned to 3a. The diastereoselectivity can be explained as follows: The (E)-enolate 2 predominantly forms in terms of a stable chelate structure to give the disilylated intermediate 6. The boat form 6a to furnish 3a is more favorable than the chair form 6b to give 3b in the transition state of the Claisen rearrangement because of the 1,3-diaxial interaction of the hydrogen and the bulky trimethysilyloxy group in 6b.

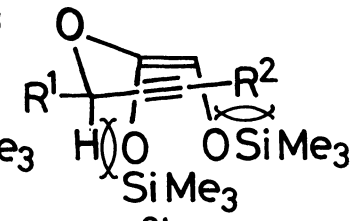


4

5a X=H, Y=CH_2OH
5b X=CH_2OH, Y=H



6a



6b

Thus highly diastereoselective synthesis of 2-hydroxy-3,4-alkadienoic acids was achieved from easily available propargyl glycolates, and the rearrangement product with allene, carboxylic acid and hydroxy functional groups is a useful precursor for the synthesis of the natural products.

References

1) M. Bertrand, J. P. Dulcere, G. Gil, J. Grimaldi, and P. Sylvestre-Panthet, *Tetrahedron Lett.*, 1976, 1507.
2) S. Musierowics and A. E. Wroblewski, *Tetrahedron*, 34, 461 (1978).
3) J. Grimaldi, *C. R. Acad. Sci., Ser. C*, 286, 593 (1978).
4) R. Gelin, M. Albrand, and S. Gelin, *C. R. Acad. Sci., Ser. C*, 269, 241 (1969).
5) J. Grimaldi and A. Cormons, *C. R. Acad. Sci., Ser. C*, 289, 373 (1979).
6) T. Sato, K. Tajima, and T. Fujisawa, *Tetrahedron Lett.*, 24, 729 (1983).
T. Fujisawa, K. Tajima, and T. Sato, *Chem. Lett.*, 1984, 1669.
T. Fujisawa, H. Kohama, K. Tajima, and T. Sato, *Tetrahedron Lett.*, 25, 5155 (1984).
7) L. Olsson and A. Claesson, *Synthesis*, 1979, 743.
8) 5a: ^{1}H NMR (CCl_4) δ 0.12 (9H, S), 1.25 (3H, d, J = 6 Hz), 1.90 (1H, br S), 3.50 (2H, m), 4.82 (2H, m), 5.92 (1H, S). 5b: ^{1}H NMR (CCl_4) δ 0.12 (9H, S), 1.18 (3H, d, J = 6 Hz), 2.50 (1H, br S), 3.50 (2H, m), 4.82 (2H, m), 5.92 (1H, S).
9) P. L. Beaulieu, V. M. Morisset, and D. G. Garratt, *Tetrahedron Lett.*, 21, 129 (1980).

(Received July 25, 1985)