Tetrahedron Letters,Vol.27,No.38,pp 4581-4582,1986  0040-4039/86 $3.00 + .00
Printed in Great Britain  Pergamon Journals Ltd.

# [2,3]WITTIG REARRANGEMENT OF 2'-ALKENYLOXYACETIC ACID ESTERS

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Summary: [2,3]Wittig rearrangement of zirconium enolates derived from alkenyloxyacetic acid esters proved to proceed with high *syn*-diastereoselectivity, high level of chirality transfer, and exclusive formation of (*Z*)-double bond.

In the preceding communication, we reported that Zr enolates of (2'*E*)-*N*-2'-alkenyloxyacetyl-*trans*-2,5-disubstituted pyrrolidines underwent [2,3]Wittig rearrangement in a highly diastereo and diastereoface selective manner.1) These selectivities seem to arise from the rigid five-membered chelate structure of the enolates containing oxygenophilic Zr atom. Therefore, it is considered that the high selectivities in the rearrangement of Zr enolates are not confined to amides but also expected from esters and other derivatives of carboxylic acids.2) We wish to describe here a highly stereoselective [2,3]Wittig rearrangement of (*E*)-alkenyloxyacetic acid ester enolates.

Some examples are shown in Table 1. In the rearrangement of isopropyl 2'-butenyloxyacetate (entries 1-4), the addition of $Cp_2ZrCl_2$ secured high *syn*-diastereoselectivity only when the (*E*)-substrate was used, similarly to the previous results obtained with the corresponding 2,5-disubstituted pyrrolidine amides.1) Experiments with optically active (*E*)-substrates bearing asymmetric carbon atom at 1'-position (entries 5-9)3) also showed the very favorable effect of added $Cp_2ZrCl_2$, where a remarkable chirality transfer as well as high *syn*-selection was observed. Furthermore, it was revealed that the configuration of double bonds newly formed in the products was exclusively *Z*. This is striking because it has been accepted that sigmatropic rearrangement usually exhibits (*E*)-selectivity.4) The high (*Z*)-selectivity can be explained as follows. As the Zr enolate forms a five-membered chelate ring, the transition state of the rearrangement is considered to take a structure like bicyclo[3.3.0]-octane (Fig. 1), where the substituent R occupies a sterically less hindered *exo*-position, leading to the formation of (*Z*)-double bond.

In view of the favorable features described above, Zr-mediated [2,3]Wittig rearrangement of esters is considered to provide one of the useful tools for stereocontrolled synthesis of chain compounds.

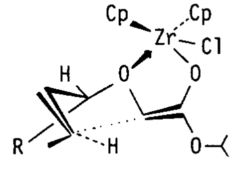

Fig. 1

The experimental procedure is exemplified below: Lithium diisopropylamide in THF (0.5 mol $dm^{-3}$, 336 µl, 1.05 eq) was added to isopropyl (1'*R*,2'*E*)-1'-butyl-2'-butenyloxyacetate (35.9 mg, 0.16 mmol) in THF (1.6 ml) at -100 °C,5) and after stirring for 1 h at -100 °C, $Cp_2ZrCl_2$ (70 mg, 1.5 eq) in THF (1.4 ml) was added. Then the mixture was stirred for 1 h at -78 °C and left to stand for 18 h at -20 °C. Under violent stirring, saturated aqueous potassium fluoride (80 µl) was added and the temperature was raised to rt. The mixture was filtered, concentrated, and purified by silica gel TLC to give isopropyl (2*S*,3*R*,4*Z*)-2-hydroxy-3-methyl-4-nonenoate [28.9 mg, 81%, $[\alpha]_D^{23}$ +8.2° (c=1.1, MeOH)].

**1** → *syn*-**2**

Table 1. [2,3]Wittig Rearrangement of Alkenyloxyacetic Acid Esters (**1**)[a]

| Entry | Starting ester (1) |  |  | Additive | Product (2) |  |  |  |  |
|---|---|---|---|---|---|---|---|---|---|
|  | R | Confn. at |  |  | Yield[b] (%) | Diastereom. ratio[d] | Confn. of *syn*-isomer |  | % ee[c] of *syn*-isomer |
|  |  | 2'-Double bond | 1'-Carbon atom |  |  | *syn* : *anti* | 4-Double bond | 3-Carbon atom[e] |  |
| 1 | H | (*Z*) |  | non | 20 | 2 : 1 |  |  |  |
| 2 | H | (*Z*) |  | $Cp_2ZrCl_2$ | 15 | 7 : 1 |  |  |  |
| 3 | H | (*E*) |  | non | 14 | 4.5 : 1 |  |  |  |
| 4 | H | (*E*) |  | $Cp_2ZrCl_2$ | 47 | 45 : 1 |  |  |  |
| 5 | Me | (*E*) |  | non | 72 | 4 : 1 | -[f] |  |  |
| 6 | Me | (*E*) | (*S*) | $Cp_2ZrCl_2$ | 91 | 100 : 1 | (*Z*)[g] | (*S*) | >96 |
| 7 | n-Bu | (*E*) | (*R*) | $Cp_2ZrCl_2$ | 81 | 61 : 1 | (*Z*)[g] | (*R*) | >96 |
| 8 | n-Oct | (*E*) | (*R*) | $Cp_2ZrCl_2$ | 70 | 90 : 1 | (*Z*)[g] | (*R*) | >96 |
| 9 | i-Pr | (*E*) | (*R*) | $Cp_2ZrCl_2$ | 26 | 50 : 1 | (*Z*)[g] | (*R*) | >96 |

a) Reaction conditions; see the text and reference 5. b) Isolated yield. c) Determined by $^1$H NMR (90 MHz) under the presence of a chiral shift reagent, Eu(hfc)$_3$. d) Determined by $^1$H NMR. e) For the determination of configuration, the product was converted into the corresponding α-methylcarboxylic acid by successive catalytic hydrogenation, LAH reduction, and $RuO_4$ oxidation, and the sign of optical rotation was compared with the authentic datum. f) A mixture of E/Z= ca. 6/4. g) Determined by $^1$H NMR. No (*E*)-isomer was detected.

This work was supported in part by a Grant-in-Aid for Scientific Research (No. 59470020) from the Ministry of Education, Science, and Culture, Japan. The authors also thank Professor T. Nakai of the Department of Chemical Technology, Tokyo Institute of Technology, for his valuable informations and discussion on this subject.

## References and Notes

1) M.Uchikawa, T.Hanamoto, T.Katsuki, and M.Yamaguchi, preceding communication on this issue. 2) [2,3]Wittig rearrangement of Li enolates derived from 2'-alkenyloxyacetic acid has been reported to give a moderate stereoselectivity; T.Nakai, K.Mikami, S.Taya, Y.Kimura, and T. Mimura, Tetrahedron Lett., **22**, 69 (1981). 3) Optically active secondary alcohols obtained by asymmetric epoxidation [T.Katsuki and K.B.Sharpless, J. Am. Chem. Soc., **102**, 5974 (1980); V.S.Martin, S.S.Woodard, T.Katsuki, Y.Yamada, M.Ikeda, and K.B.Sharpless, ibid, **103**, 6237 (1981)] were converted into 2'-alkenyloxyacetic acids by Nakai's procedure (reference 2). 4) One (*Z*)-selective example has been reported with a substrate having a trisubstituted double bond; W.C.Still and A.Mitra, J. Am. Chem. Soc., **100**, 1927 (1978). 5) At -78 °C, Li enolates rearrange to some extent resulting in the decrease of diastereoselectivity.

(Received in Japan 27 May 1986)