Tetrahedron Letters,Vol.27,No.35,pp 4185-4188,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

ASYMMETRIC [2,3]WITTIG REARRANGEMENT INVOLVING CHIRAL POTASSIUM AZAENOLATES. THE DRAMATIC INFLUENCE OF THE POTASSIUM COUNTERION AND ITS COMPLEXATION WITH 18-CROWN-6

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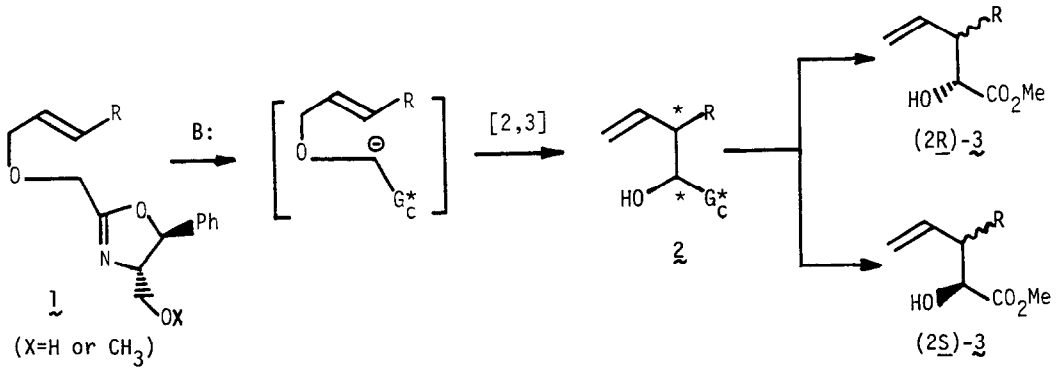
SUMMARY: The diastereoface selection is described in the title rearrangement of chiral 2-oxazoline systems either in the absence or the presence of 18-crown-6. The dramatic effects of the K^+ counterion and its complexation with the crown ether are noted.

In view of the tremendous advance in the development of chiral enolates and their utilities in asymmetric aldol and alkylation reactions,[1] the asymmetric [2,3]Wittig rearrangement involving a chiral enolate as the migrating terminus should constitute a new, general strategy for asymmetric carbon-carbon bond formations. In an effort to develop the asymmetric [2,3]Wittig variant using Meyers' 2-oxazoline ring as the chiral auxiliary,[2] we have recently reported that the lithium azaenolate rearrangement of chiral oxazolines 1 (X=CH_3) eventually affords the α-hydroxy ester 3 with (R)-configuration in 38-78% enantiomeric excess.[3] In a continuation of these studies, we have now found that treatment of 1 (X=H) with potassium hydride (2 equiv) induces the [2,3]-shift either in the absence or the presence of 18-crown-6. Disclosed here are the intriguing stereochemical observations in these potassium azaenolate rearrangements.



1 (X=H or CH_3) 2

a, R=H; b, R=CH_3; c, $(CH_3)_2C=CHCH_2-O-CH_2-G^*_c$

The dianionic rearrangement of oxazolines 1 (X=H) was carried out in THF using two equivalent of potassium hydride at 15-20 °C[4] and at -20 °C in the presence of 18-crown-6. Usual work-up afforded essentially quantitative yields of the rearranged products 2 which were then converted to the hydroxy esters 3 according to the reported procedures.[2,3] The absolute configuration of 3 was assigned as described in our previous paper.[3,5] Table 1 summarizes the stereochemical results.

Several significant trends are evident from the data in the table. (1) The KH-induced rearrangement in the absence of 18-crown-6 exhibits the opposite sense of diastereoface selection to that in the BuLi-induced counterpart.[3] In contrast, however, the addition of 18-

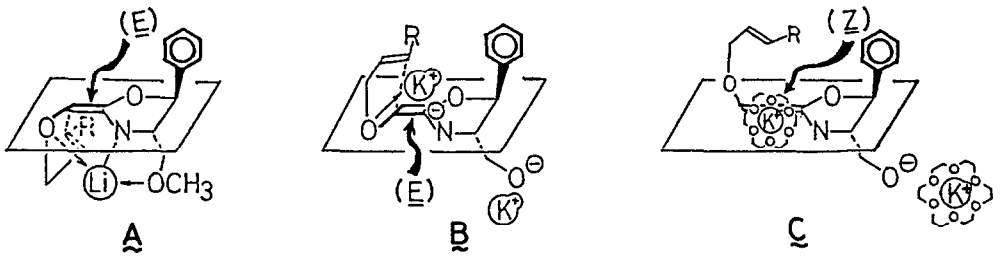
Table 1. The Chiral α-Hydroxy Esters (3) via KH-induced Rearrangement of 1 (X=H)

Substrate	Base System	Erythro : Threo[a]	%ee[b]	Config.
1a[c,d]	KH		84[e]	2S
1b (93% E)[f]	KH	41 : 59	Erythro 0 Threo 74	 2S
1b (93% Z)	KH	43 : 57	Erythro 64 Threo 78	2S 2S
1c	KH		56	2S
1a	KH/18-Crown-6		96[e]	2R
1b (93% E)[g]	KH/18-crown-6	46 : 54	Erythro 86 Threo 84	2R 2R
1b (93% Z)	KH/18-Crown-6	54 : 46	Erythro 86 Threo 86	2R 2R
1c	KH/18-Crown-6		82	2R

[a] Determined by GLC and NMR assays as described in ref. 3. [b] Determined by NMR assay using (+)-Eu(DPPM)$_3$ as a chiral shift reagent: cf. H. Kawa, F. Yamaguchi, and N. Ishikawa, Chem. Lett., 1982, 153. [c] The rearrangement with 2 equiv of BuLi at -85 °C provided (2R)-3a in only 8% ee. [d] The monoanionic rearrangement of 1a (X=CH_3) with KH at 20 °C provided only 6% ee. [e] Refers to % ee for the α-methoxy ester of 3a. [f] The rearrangement with 2 equiv of BuLi at -85 °C provided a stereo-mixture (erythro : threo = 89 : 11). The major erythro-product afforded 0% ee. [g] The use of $KN(SiMe_3)_2$ in stead of KH provided essentially the same stereo-mixture (erythro : threo = 54 : 46) along with a comparable level of % ee.

crown-6 surprisingly exhibits a further reversal of the π-facial selection. (2) In both the KH- and KH/crown-induced rearrangements, the introduction of methyl group(s) on the allylic moiety results in a significant and gradual decrease in diastereoface selection; the trends are opposite to that reported for the BuLi-induced counterpart.[3] (3) Unfortunately, the diastereoselectivity observed in the present rearrangements of 1b (X=H) pair are much lowered than that (90% erythro) observed in the BuLi-induced counterpart of (E)-1b (X=CH_3).[3]

These trends have no definitive explanations mainly because any information pertaining to the structure of the K-azaenolate is not available.[6] Nontheless, the dramatic changeovers in diastereoface selection by changing the counterion from Li^+ to K^+ and by complexation of K^+ with 18-crown-6 are reasonably explicable as follows. The trend (2) described above strongly suggests that both the KH- and KH/crown-induced rearrangement occur predominantly from the top-side of the enolate system where the steric repulsion between the allyloxy moiety and the phenyl is operative. This is in direct contrast to the BuLi-induced counterpart which proceeds preferentially from the bottom-side of the metal-chelated (E)-enolate as shown in the formula A. Thus, the (2S)-selectivity in the KH-induced process must be visualized by the formula B where the enolate-K^+ ion is favorably located in the top-side (Si-face) of the still chelated (E)-enolate[7] to avoid the dicationic repulsion. In the KH/crown-induced process, on the other hand, the [2,3]-shift might be considered to proceed preferentially from the top-side (Re-face) of the non-chelated (Z)-enolate (see formula C) where the steric repulsion between the allyloxy moiety and the "octopus arms" of 18-crown-6 would be minimized.[8]



In summary, the KH-induced rearrangement of chiral oxazolines in the absence or the presence of the crown ether have shown to afford either (S)- or (R)-α-hydroxy acid derivatives in relatively high enantiomeric excess, thus making it potentially useful for complementary asymmetric synthesis.[9] Furthermore, the results of this work demonstrate the dramatic effects of potassium cation and its complexation with 18-crown-6 on the diastereoface selection in the asymmetric [2,3]Wittig rearrangement. Further effort is now in progress to develop asymmetric [2,3]Wittig variants involving different chiral enolates.

Acknowledgment: This research was generously supported by the Grant-in-Aid for Scientific Research from the Ministry of Education, Japan.

References and Notes

1. Recent reviews: a) "Asymmetric Synthesis", ed. by J. D. Morrison, Academic Press, New York (1984), Vol. 3, Chap. 1-4; b) D. A. Evans, J. V. Nelson, and T. R. Taber, Top. Stereochem., 13, 1 (1982).
2. Reviews: a) M. Reuman and A. I. Meyers, Tetrahedron, 41, 837 (1985); b) K. A. Lutomski and A. I. Meyers, in ref 1a, Chap. 3.
3. K. Mikami, K. Fujimoto, T. Kasuga, and T. Nakai, Tetrahedron Lett., 25, 6011 (1984).
4. At 0 °C, the rearrangement did not proceed to an appreciable extent.
5. K. Mikami, O. Takahashi, T. Kasuga, and T. Nakai, Chem. Lett., 1985, 1729.
6. In order to gain information on the K-azaenolate geometry, we attempted alkylation and silylation of 2-methoxymethyl oxazoline using KH. Unfortunately, all attempts to trap the K-azaenolate failed, instead resulting in the recovery of the starting material.
7. A similar 5-membered chelation of K^+ with an alkoxy group has been amply reported: e.g. T. J. Prosser, J. Am. Chem. Soc., 83, 1701 (1961); C. C. Price and W. H. Snyder, Ibid., 83, 1773 (1961).
8. In order to confirm the (Z)-enolate formation in the presence of 18-crown-6, we carried out the [2,3]Wittig shift of 2-(prenyloxy)methyl oxazoline derived from (1S, 2R)-(+)-norephedrine where the bottom-side rearrangement should be favored since the top-side is blocked by both the methyl and phenyl groups. The rearrangement was found to exhibit the (2S)-selection (56% ee), thus indicating the preferable formation of the (Z)-azaenolate.
9. For a list of recent examples of complementary asymmetric synthesis, see: K. Tomioka, K. Ando, Y. Takemasa, and K. Koga, Tetrahedron Lett., 25, 5677 (1984).

(Received in Japan 31 May 1986)