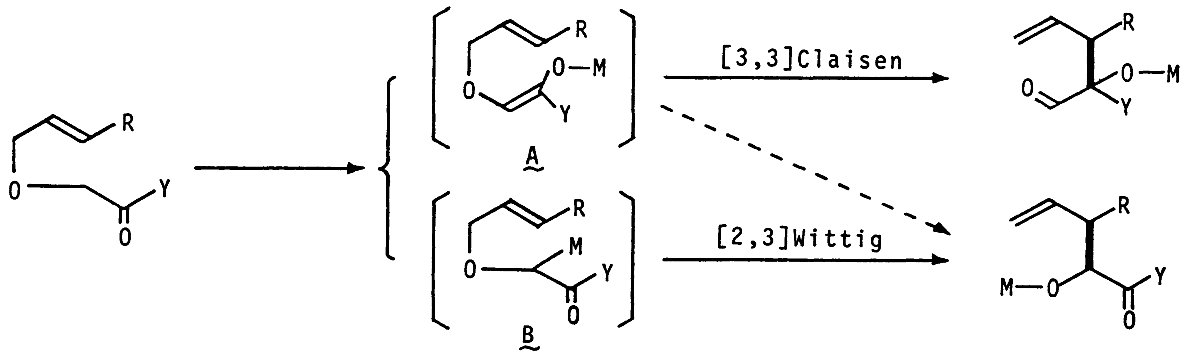
CHEMISTRY LETTERS, pp. 1599-1602, 1986.

[2,3]Wittig Rearrangements of "Lithium Enolates" Generated from α-Allyloxy Esters, Ketones, and Oximes. Some Implications of the Enolate Structures

Osamu TAKAHASHI, Takahiro SAKA, Kōichi MIKAMI, and Takeshi NAKAI*
Department of Chemical Technology, Tokyo Institute of Technology,
Ookayama, Meguro-ku, Tokyo 152

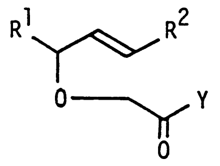
The lithium ester and ketone enolates (generated in HMPA-THF) and the dilithiated oxime (generated in THF) are shown to serve well as the migrating terminus for the [2,3]Wittig shift, not for the [3,3]Claisen shift. On the basis of these observations, the solution structures of the "lithium enolates" are discussed.

Much attention has recently been focused on the sigmatropic rearrangement of "metal enolates" of α-allyloxy carbonyl systems, where the two competing modes of sigmatropic shifts are conceivable (Scheme 1).$^{1-4)}$ Of the two possible forms, the *O*-metalated species (**A**) may be envisioned as a 3-oxa-1,5-diene which can undergo the [3,3]Claisen shift, whereas the *C*-metalated species (**B**) may be viewed as an (allyloxy)carbanion which can, in contrast, undergo the [2,3]Wittig shift. Thus, studies on such enolate rearrangements would provide a unique opportunity of gaining an insight into the solution structures of metal enolates concerned.

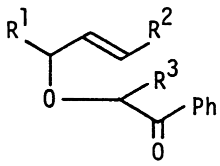


Scheme 1.

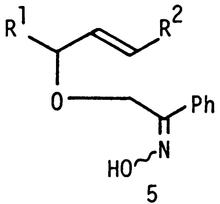
Recently we have reported that the lithium enolates of acid **1**$^{1)}$ and amide **2**$^{2)}$ (generated with LDA$^{5)}$ in THF) undergo the [2,3]Wittig shift at *ca*. -80 °C, whereas the lithium enolate of ester **3** generated in the same manner *does not* undergo either shift under similar conditions.$^{3a)}$ In marked contrast, Koreeda has reported that the lithium enolate of ketone **4'** (generated with LiH in THF-MeOH) undergoes mainly the [3,3]Claisen shift along with the [2,3]Wittig shift (20%) at 67 °C, while the potassium counterpart undergoes exclusively the [3,3]Claisen shift.[4] These remarkably varied observations prompted us to investigate the rearrangement behaviors of lithium enolates termini generated under different conditions. This report discloses that the lithium enolates of ester 3 and ketone 4, when generated in HMPA-THF, undergo exclusively the [2,3]Wittig shift at -70 °C and that the dilithium species of oxime 5 also undergoes the facile [2,3]Wittig shift.



1, Y = OH; 2, Y = N; 3, Y = OCH_3



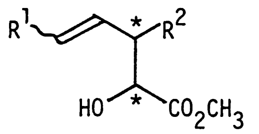
4, R^3 = H; 4', R^3 = CH_3



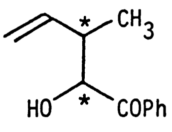
5

First, we examined the rearrangement behavior of the lithium enolate of ester 3 generated in HMPA-THF. Thus, 3a (R^1=CH_3, R^2=H) was treated with LDA in HMPA-THF (1 : 4 by vol.) at -70 °C and stirred at that temperature for several hours. At this point, the substrate almost disappeared (monitored by TLC). Then, the reaction mixture was slowly warmed to 0 °C to afford an 80% isolated yield of the [2,3]Wittig product (6a) as the sole product with 75% of (E)-selectivity.[6] Likewise, (E)-3b (R^1=H, R^2=CH_3) provided 6b with an extremely high erythro-selectivity (96%).[6] The remarkably enhanced [2,3]Wittig reactivity of the lithium enolate terminus generated in HMPA-THF is in stark contrast to the extremely low reactivity of that generated in THF,[3a] indicating that the added HMPA would strongly coordinate with Li^+ to form a solvent-separated or free enolate with the enhanced carbanion reactivity.[7] This is fully consistent with the previous observations that silylation of the former Li-enolate affords selectively the C-silylated form,[3a] whereas silylation of the latter Li-enolate provides exclusively the O-silylated form as usual.[3]

Second, we found that the lithium enolate of ketone (E)-4b (R^1=H, R^2=CH_3), when generated in HMPA-THF at -70 °C and then allowed to warm to 0 °C (vide supra), underwent exclusively the [2,3]Wittig shift to yield the hydroxy ketone 7b in 45% yield[8] and in 69% of erythro-selectivity.[9] The exclusive occurrence of the [2,3]Wittig shift in the presence of HMPA is in direct contrast to the preferential occurrence of the [3,3]Claisen shift in the absence of HMPA,[4] thus suggesting that the carbanion reactivity of the lithium enolate would be greatly enhanced by the strong coordination of HMPA with Li^+ as descrived above.[7]

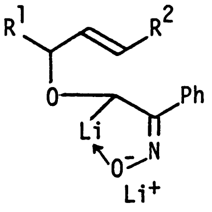


6a, R^1 = CH_3, R^2 = H; 6b, R^1 = H, R^2 = CH_3

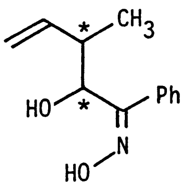


7b

Third, we studied the LDA-induced rearrangement of both the syn- and anti-oxime 5b (R^1=H, R^2=CH_3),[10] where the exclusive occurrence of the [2,3]Wittig shift is highly anticipated in view of the *C*, *O*-dilithiated chelate structure (8) widely accepted for the dilithiated species.[11] We found that the dilithiated species generated from either syn- or anti-5b with LDA in THF underwent the [2,3]-Wittig shift at 0 °C to provide 57-78% of the identical [2,3]Wittig product (9b) with exactly the same erythro-purity (65%)[12] and exclusively the syn-oxime geometry as depicted below, independent of the oxime geometry of 5b.[13] These observations strongly support the intermediacy of the chelate species (8)[14] which should exhibit an extremely high carbanion reactivity.

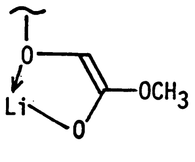


8

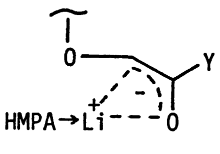


Syn-9b

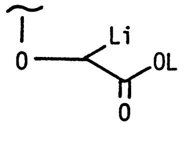
These observations outlined above, coupled with the previously-reported ones on the closely related lithium enolate termini, allow us to delineate the solution structures of "lithium enolates" concerned, particularly the contribution of the *C*-metalated species (*cf.* B in Scheme 1) to the overall enolate structure and the state of the ion pairing thereof. For instance, the low [2,3]Wittig reactivity of the ester Li-enolate terminus generated in THF provides an evidence in support of the *O*-lithiated chelate structure (10) as widely postulated,[15] whereas the relatively high [2,3]Wittig reactivity of the Li-enolates generated in the presence of a dissociating solvent such as HMPA might suggest the solvent-separated or free enolate structure (11).[7] As for the dilithiated species of acid 1 generated in THF, on the other hand, it appears likely that this species would adopt at least partially the *C*-lithiated structure (12) in view of the previously-reported high [2,3]Wittig reactivity.[1]



10



11 (Y = OCH_3, Ph)



12

In summary, this work has demonstrated that the Li-enolates of α-allyloxy esters and ketones, when generated in HMPA-THF, exhibit an entirely different behavior from those generated in THF to undergo exclusively the [2,3]Wittig shift and that the *C*, *O*-dilithiated species of the oxime counterpart also undergoes the facile [2,3]Wittig shift. Further works are in progress on the [3,3]Claisen *vs.* [2,3]Wittig shift in different enolate rearrangements.

References

1) T. Nakai, K. Mikami, S. Taya, Y. Kimura, and T. Mimura, Tetrahedron Lett., 22, 69 (1981).

2) K. Mikami, O. Takahashi, T. Kasuga, and T. Nakai, Chem. Lett., 1985, 1729. *cf*. M. Uchikawa, T. Hanamoto, T. Katsuki, and M. Yamaguchi, Tetrahedron Lett., in press.

3) a) O. Takahashi, T. Maeda, K. Mikami, and T. Nakai, Chem. Lett., in press; b) S. Raucher and L. M. Gustavson, Tetrahedron Lett., 27, 1557 (1986). The two groups have reported that the ketene silyl acetals of **3** undergo exclusively the [3,3]Claisen shift at 110 °C.

4) M. Koreeda and J. I. Luengo, J. Am. Chem. Soc., 107, 5572 (1985). In contrast, the potassium enolate of a similar ketone to **4** (generated with *t*-BuOK in *t*-BuOH) has been shown to undergo exclusively the [2,3]Wittig shift by A. F. Thomas and R. Dubini [Helv. Chim. Acta, 57, 2084 (1974)]. The reasons for this discrepancy remain unclear.

5) Abbreviations: LDA = lithium diisopropylamide, THF = tetrahydrofuran, HMPA = hexamethylphosphoramide.

6) The structure was elucidated through spectral comparisons with the authentic sample [(*E*)- or erythro-rich] which was prepared from the [2,3]Wittig product of acid **1** via treatment with CH_2N_2.

7) It should be considered that the enolate [2,3]Wittig shift proceeds at much lower temperature than the enolate [3,3]Claisen shift in general.

8) The relatively low yield is apparently due to the subsequent aldol reaction of the product ketone with the enolate.

9) ^1H NMR ($CDCl_3$), δ 0.77 (erythro-CH_3) and 1.23 (threo-CH_3). The stereochemical assignment was made on the basis of spectral comparisons of its diol derivative prepared via Grignard reaction of **7b** and excess PhMgBr with an authentic sample (erythro-rich) which was independently prepared from ester **6b** in the same manner.

10) The syn- and anti-oxime were separated by chromatography: ^1H NMR ($CDCl_3$), δ 4.67 and 4.32 for the α-methylene of syn- and anti-**5b**, respectively.

11) a) W. G. Kofron and M.-K. Yeh, J. Org. Chem., 41, 439 (1976); b) A. Streitwieser, Jr., Acc. Chem. Res., 17, 353 (1984).

12) The structure was elucidated by its conversion to ketone **7b** by treatment with acetone (a large excess) in the presence of HCl at 20 °C.

13) This means that the dilithiation process of anti-**5b** should involve an anti→syn isomerization to form the syn-chelate species (**8**); *cf*. M. E. Jung, P. A. Blair, and J. A. Lowe, Tetrahedron Lett., 1976, 1439.

14) Alternatively, the ion cluster structure[11b)] is equally consistent with our results.

15) M. Nagatsuma, F. Shirai, N. Sayo, and T. Nakai, Chem. Lett., 1984, 1393, and references cited therein.

(Received July 16, 1986)