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ASYMMETRIC INDUCTION IN THE [2,3]WITTIG REARRANGEMENT OF ALLYLIC ETHERS WITH A CHIRAL SUBSTITUENT. NEW ENTRIES TO STEREOCONTROL OVER THREE CONTIGUOUS CHIRAL CENTERS

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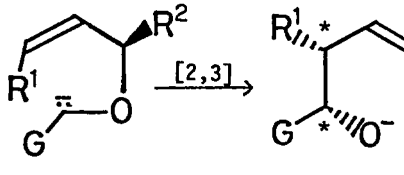
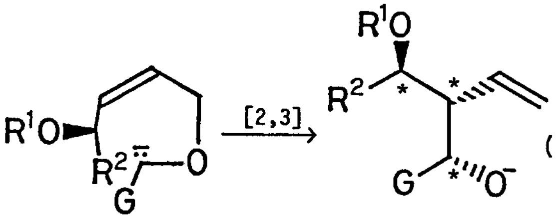
Summary: The [2,3]Wittig rearrangements of allylic ethers with a chiral substituent at the γ-positions, derived from (*S*)-lactaldehyde and (*R*)-glyceraldehyde, are shown to exhibit an extremely high asymmetric induction, together with a high simple diastereoselectivity.

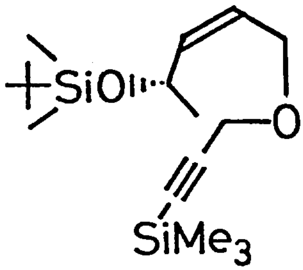
Recently the asymmetric [2,3]Wittig rearrangement termed "asymmetric transmission type" (eq 1) has widely been utilized for asymmetric synthesis of acyclic frameworks.[1] In an effort to further enhance the potential of the [2,3]Wittig technology, we have now investigated a conceptually new type of asymmetric version, termed "asymmetric induction type" (eq 2), wherein an allylic ether with a chiral substituent at the γ-position is employed as the substrate. A major stereochemical problem here is associated with asymmetric induction by the chiral substituent (diastereofacial selection), which remains largely unexplored.[2] Herein we report that the [2,3]Wittig rearrangement of the allylic ethers of type 1 and 2 exhibits an extremely high level of both asymmetric induction and simple diastereoselectivity, thus providing new entries to stereocontrol over the three contiguous chiral centers.



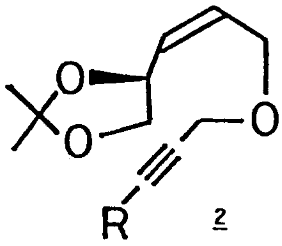
(1)



(2)



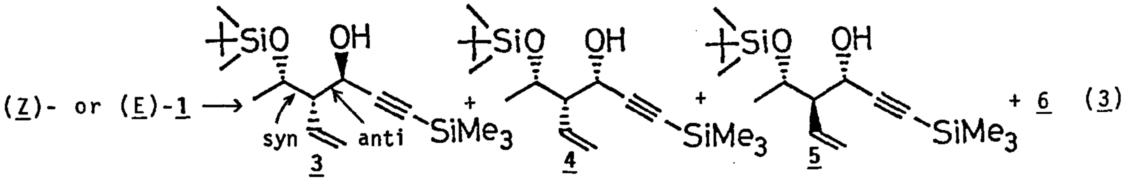
1

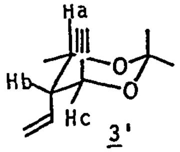


2

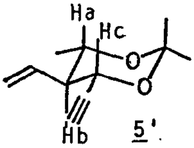
a, R = $SiMe_3$
b, R = CH_3

In this work, we selected the acetylenic groups as the key G group based on our previous observation that such groups generally provide a high degree of simple diastereoselection in the [2,3]Wittig processes.[3] First, (Z)- and (E)-1 were selectively prepared from (S)-lactaldehyde via the usual sequence[4] and each was subjected to the carbanion rearrangement under the standard conditions [n-BuLi (1.2 equiv), THF, -78°C, 5 h] (eq 4). The stereochemistry of the products was deduced from 500 MHz NMR spectra of their acetonides prepared by usual desilylation/acetonidation sequence. The most informative are the coupling constants as exemplified below. The results thus observed are shown in Table 1 (entries 1-3).





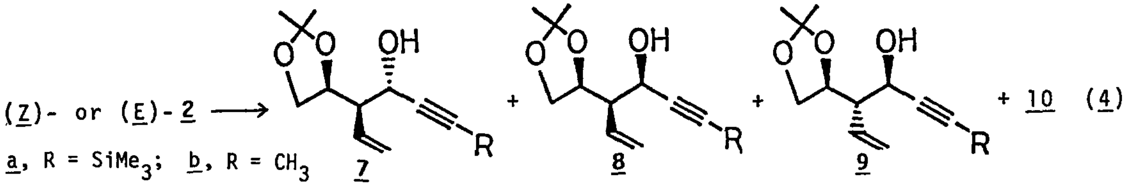
Jab = 3.8 Hz
Jbc = 4.6 Hz

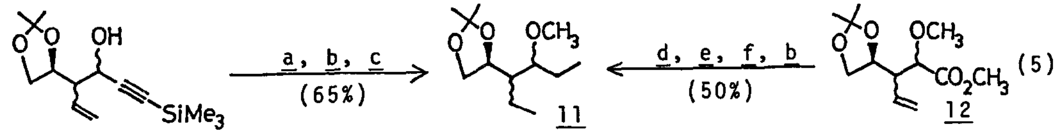


Jab = 10.7 Hz
Jbc = 10.7 Hz

The most striking feature of this rearrangement is the remarkably high asymmetric induction (>95% 4,5-syn) observed with (Z)-1, along with an extremely high 3,4-anti diastereoselectivity. Also notable is that (E)-1 shows the opposite sense of asymmteric induction, although the degrees are lowered (entry 2 and 3).

Second, the Z/E pairs of 2a and 2b were selectively prepared from (R)-glyceraldehyde acetonide[5] and each was subjected to the carbanion rearrangement as described above (eq 4). The stereochemical assignments of the major products (7a and 8a) were made through HPLC[6] comparisons of their derivative (11) with the authentic samples independently prepared from the stereochemically-defined Claisen products (12)[7] (eq 5).





a n-Bu$_4$NF ; b H$_2$/PtO$_2$: c KH/CH$_3$I ; d LiAlH$_4$; e (COCl)$_2$/DMSO/Et$_3$N ; f CH$_2$=PPh$_3$

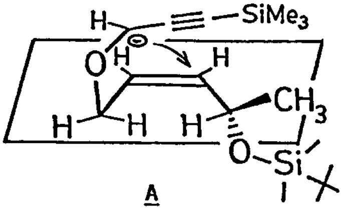
Table 1. The [2,3]Wittig Rearrangement of 1 and 2

Entry	Substrate[a]	%Yield[b]	Product Ratio[c]			
			3	4	5	6
1	(Z)-1 (97%)	77	94	1	4	1
2	(E)-1 (97%)	93	10	21	50	19
3[d]	(E)-1 (97%)	74	3	3	87	7
			7	8	9	10
4	(Z)-2a (100%)	77	>99[e]	-	-	-
5	(Z)-2b (100%)	62	98	-	-	2
6	(E)-2a (100%)	86	12	81	3	4
7	(E)-2b (100%)	73	7	77	16	-

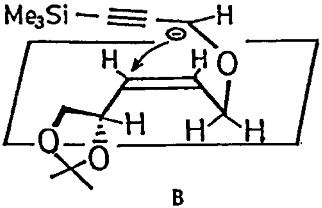
[a] The number in the parenthesis indicates the geometric purity of the substrate (determined by ^{13}C NMR assay). [b] Refers to isolated yield. [c] Determined by capillary GLC (XE 60, 30 m). [d] Run in THF-HMPA (4:1) with LDA (1.2 equiv). [e] $[\alpha]_D^{18^\circ}$ -16.2° (c 1.02, $CHCl_3$).

Table 1 (entries 4-7) shows the results thus observed. Again, a remarkably high asymmetric induction (4,5-syn) is observed with (Z)-**2a** and **2b**, together with an extremely high 3,4-anti diastereoselectivity (enties 4 and 5). Another interesting finding is that the (E)-counterparts exhibit the same sense of asymmetric induction, along with the opposite sense of simple diastereoselection (3,4-syn), although the degrees are lowered.

The high asymmetric induction observed in this work are of mechanistic and synthetic interest. While the high Z → 3,4-anti diastereo-selectivities are just what we anticipate from previous works,[1,3] the Z → 4,5-syn diastereofacial selections can be visualized by the transition state **A** and **B**. The oxy-substituents at the chiral centers are perpendicular to the plane of the double bond to avoid the allylic 1,3-repulsion[8] and the cabanion attacks preferentially from the opposite site to the oxy-substituent, thus leading to the high 4,5-syn selection.[9]



A



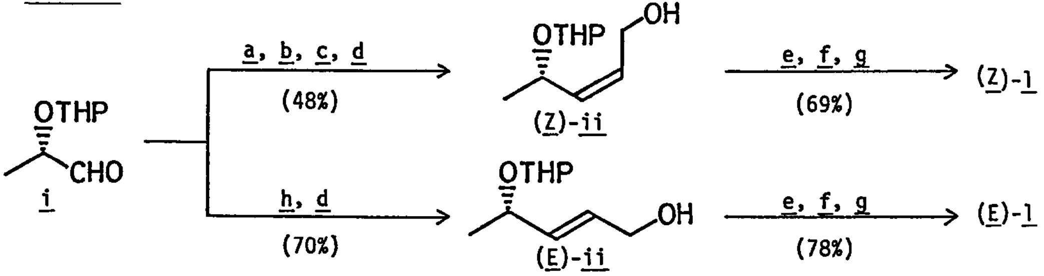
B

In summary, we have demonstrated that the [2,3]Wittig rearrangements of the allylic ethers of type 1 and 2 provide an extremely high level of asymmetric induction, together with a high simple diastereoselectivity. Thus, the high degree of stereocontrol, coupled with the unique multi-functionality of the products, makes the present asymmetric version an attractive method for stereo-control over the three contiguous chiral centers. Applications of this methodology in natural product synthesis are now in progress in our laboratory.

Referances and Notes

1) Review; T. Nakai and K. Mikami, Chem. Rev., 86, 885 (1986).
2) After completion of this work, R. Bruckner and H. Priepke [Angew. Chem. Int. Ed. Engl., 27, 278 (1988)] have reported a similar type of asymmetric [2,3]Wittig variants of the glyceraldehyde-derived allylic ethers (G = H and CO_2Me) which provide a high asymmetric induction, though the yield of the latter is low (40%).
3) T. Nakai, K. Mikami, S. Taya, and Y. Fujita, J. Am. Chem. Soc., 103, 6492 (1982). K. Mikami, K. Azuma, and T. Nakai, Tetrahedron, 40, 2303 (1984).
4) Scheme 1 outlines the synthetic sequences for (Z)- and (E)-1 from the THP-protected lactaldehyde (i). The conversions of i to the (Z)- or (E)-ii were made following the Sharpless procedures: T. Katsuki, A. W. M. Lee, P. Ma, V. S. Martin, S. Masamune, K. B. Sharpless, D. Tuddenham, F. J. Walker, J. Org. Chem., 47, 1373 (1982).

Scheme 1



^{a} $CBr_4/Zn/PPh_3$; ^{b} n-BuLi/$ClCO_2CH_3$; ^{c} H_2/Lindlar's cat. ; ^{d} DIBAL-H ;
^{e} aq.NaOH/CH=CCH_2Br/TBAI(cat.) ; ^{f} TBSCl/imidazole ; ^{g} n-BuLi/TMSCl ;
^{i} $(EtO)_2P(O)CH_2CO_2Et$/NaH

5) The synthetic sequences are essentially the same as outlined in Scheme 1.
6) Column : Zorbax SIL ; Solvent : hexane/AcOEt (19 : 1).
7) J. K. Cha and S. C. Lewis, Tetrahedron Lett., 25, 5263 (1984). The stereochemical determinations of 7b-10b were made based on their GLC similarities to those of 7a-10a.
8) J. K. Cha, W. J. Christ, Y. Kishi, Tetrahedron, 40, 2247 (1984).
9) For a similar, more detailed mechanistic argument, see ref. 2.

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