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SILOXY-[2,3]WITTIG REARRANGEMENT: A NEW METHOD FOR DIASTEREOSELECTIVE PREPARATIONS OF 1,2-DIOL SYSTEMS

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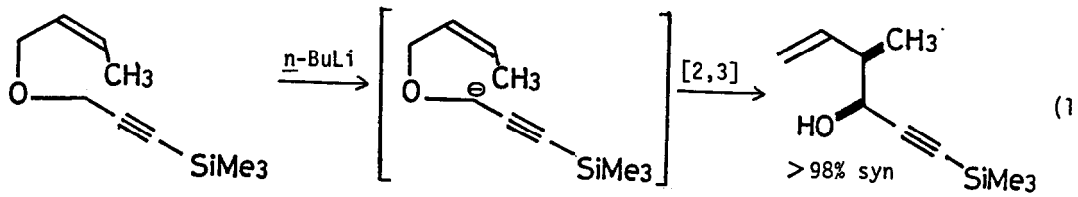
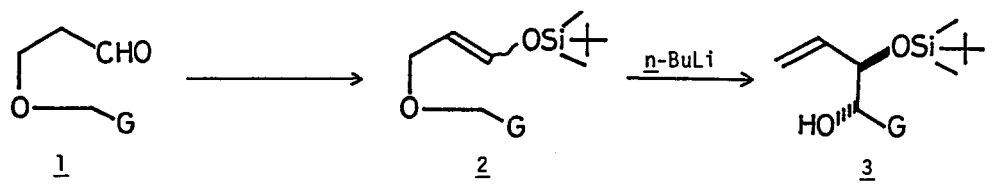
Summary: A novel [2,3]Wittig variant, termed "siloxy-[2,3]Wittig rearrangement", has been developed which provides the half-silylated 1,2-diol systems with a high anti-diastereoselectivity. The unusual anti-selectivity is discussed on mechanistic grounds.

The [2,3]Wittig sigmatropic rearrangement has become an efficient method for acyclic stereocontrol since we developed highly diastereoselective variants as exemplified in eq. 1.[1,2] In an effort to further expand the synthetic scope of the [2,3]Wittig technology, we have now investigated the feasibility of a novel variant, termed "siloxy-[2,3]Wittig rearrangement", which employs a γ-(silyloxy)allyl ether system (2) as the substrate and might produce a stereochemically-defined 1,2-diol system (3) of synthetic interest (eq. 2).[3] Our major concern is how the γ-siloxy substituent could influence or control the stereochemistry of the rearrangement. We now report that the siloxy-[2,3]Wittig variant proceeds smoothly to provide the 1,2-diol systems with a high diastereo-selectivity and that its stereochemical course is quite different from that of the usual [2,3]Wittig rearrangement.



(1)



(2)

1 2 3

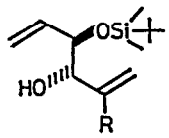
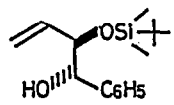
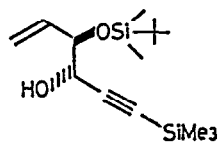
a, G = CH=CH$_2$; b, G = C(CH$_3$)=CH$_2$
c, G = C$_6$H$_5$; d, G = C≡C-SiMe$_3$

The starting aldehydes (1a-d) were prepared from THP-protected 3-bromo-1-propanol by the simple three-step operation, i.e., etherification with an alcohol (GCH_2OH), deprotection, and Swern oxidation.[4] The requisite substrates (2a-d) were obtained in 63-80% isolated yields as Z/E mixtures via silylation of the corresponding aldehyde (1) with t-butyldimethylsilyl trifrate under the usual conditions (Et_3N, CH_2Cl_2, 5 °C, 5-10 min).[5] In all cases, the thermodynamically more stable Z-isomer was favored, ranging from 65% Z for 2d to 71% Z for 2c (see Table 1).[6] The carbanion rearrangements of 2a-d were carried out by the standard procedure [n-BuLi (1.2 eqiv.), THF, -78 ∿ -65 °C, 5 h] to afford the half-silylated 1,2-diols (3) in moderate-to-high yields. It is noteworthy that these rearrangements were significantly slower than the usual [2,3]Wittig rearrangements, as expected from the frontier orbital consideration.[3] The stereochemical assignments of the products were made through their conversions to the known compounds.[7] Table 1 summarizes the stereochemical outcomes thus observed.

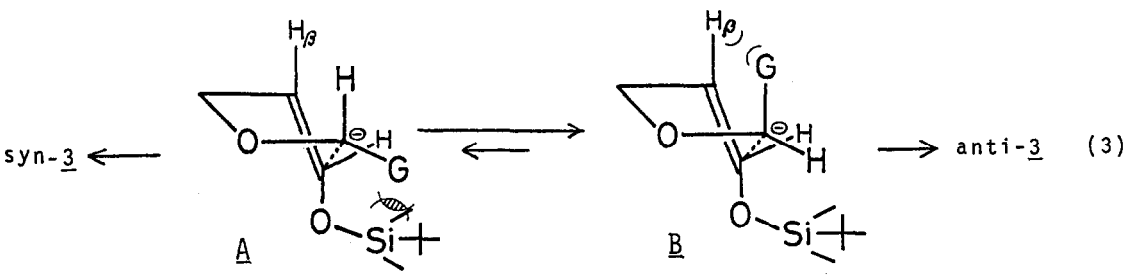
Inspection of the data in Table 1 reveals significant stereochemical features of the present variant. The most notable is that these rearrangements of the Z-rich substrates exhibit a high anti-diastereoselection; this is in direct contrast to the high Z⟶syn selection widely observed for the usual [2,3]Wittig rearrangements (cf. eq. 1).[1,2] More surprisingly, an increase in Z-content of the substrate results in a lowered anti-selectivity (entry 3 vs. 4 and entry 5 vs. 6). These unexpected results indicate that both the rearrangements of the Z- and E-substrates exhibit the same anti-selection, the latter providing a higher selectivity. Of particular interest is entry 5, where both the Z- and E-substrates provide an extremely high anti-selectivity, thus leading to the almost exclusive formation of anti-3d, irrespectative of the low geometric purity of the substrate used.

The Z⟶anti selection generally observed here is quite exceptional and of mechanistic interest, whereas the E⟶anti selection is quite normal and readily explicable in terms of the transition-state model previously advanced.[1,8] The Z⟶anti selection is reasonably rationalized as a result of the special situation that the introduction of the bulky γ-siloxy group would greatly enhance the gauche repulsion between the siloxy group and G group in the transition state A which prevails over the 1,3-repulsion between H_β and G in the transition state B (eq. 3). In other words, the transition state such as A with G group at the pseudo-equatorial position, which is generally favored for the usual [2,3]Wittig variants, is greatly disfavored for the present siloxy-[2,3]Wittig variant.

Table 1. The Siloxy-[2,3]Wittig Rearrangement

Entry	Substrate (2)	Z : E[a]	Product (3)	anti : syn[b]	%yield[c]
1	2a, G = $CH{=}CH_2$	70 : 30		95 : 5	53
2	2b, G = $C(CH_3){=}CH_2$	70 : 30		91 : 9	74
3	2c, G = C_6H_5	71 : 29		82 : 18	73
4		93 : 7[d]		77 : 23	81
		[Z → 74% anti; E → 100% anti][e]			
5	2d, G = $C{\equiv}C\text{-}SiMe_3$	65 : 35		98 : 2	79
6		95 : 5[f]		95 : 5	66
		[Z → 97% anti; E → 100% anti][e]			

[a] Determined by ^1H NMR analyses (ref 6). [b] Determined by ^{13}C NMR for 3a and 3b, HPLC (Zorbax SIL, hexane/AcOEt) for 3c, and capillary GLC (XE 60, 30 m) for 3d. For the stereochemical assignments, see ref 7. [c] Refers to the isolated yield after column chromatography. [d] This substrate was prepared via the silylation carried out in CCl_4 at 0 °C for 45 h. (equilibrating conditions), although the yield was lower (32%). [e] Stands for the calculated selectivity based on 100% of geometric purity of either (E)- or (Z)-substrate. [f] This subtrate was obtained by column chromatographic separation of the Z/E mixture.



In summary, we have developed a novel [2,3]Wittig variant, termed "siloxy-[2,3]Wittig rearrangement", which provides the half-silylated 1,2-diol systems with a relatively high anti-diastereoselectivity, independent of the geometry of the substrates. The high stereoselectivity, coupled with the unique multifunctionality of the rearrangement products, makes this siloxy-[2,3]Wittig variant potentially useful for the synthesis of polyhydroxylated natural products. Further works along this line are under way in our laboratory.

References and Notes

1) Review; T. Nakai and K. Mikami, Chem. Rev., 86, 885 (1986).

2) T. Nakai, K. Mikami, S. Taya, and Y. Fujita, J. Am. Chem. Soc., 103, 6492 (1981); K. Mikami, K. Azuma, and T. Nakai, Tetrahedron, 40, 2303 (1984).

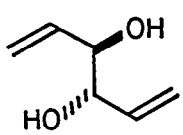
3) A frontier orbital consideration tells us that the introduction of a γ-siloxy substituent would make the [2,3] shift slower since the siloxy group substantially raises the LUMO of the olefine part, thus making the interaction of the LUMO (olefin) and the HOMO (carbanion) less effective: I. Fleming, "Frontier Orbitals and Organic Chemical Reactions", John Wiley & Sons: London, 1976.

4) In the case of 1d (G= C≡C-$SiMe_3$), however, the deprotection/Swern oxidation sequence was performed after silylation (EtMgBr→Me_3SiCl, THF) of the ether obtained by etherification with propargyl alcohol.

5) Review: H. Emde, Synthesis, 1982, 1. It is noteworthy that trimethylsilyl trifrate cannot be used here because trimethylsilyl enol ethers are known to undergo the transmetalation with an alkyllithium: G. Stork and P. H. Hudrik, J. Am. Chem. Soc., 90, 4462, 4464 (1968): H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, J. Org. Chem., 34, 2324 (1969): T. Wakamatsu, K. Akasaka, and Y. Ban, ibid, 44, 2008 (1979).

6) The Z- and E-isomers of the silyl enol ethers (2) are clearly distinguishable by ^1H NMR spectra ($CDCl_3$). In all cases, the Z-isomers show a doublet due to the γ-olefinic proton at a higher field (δ 6.23-6.32) as compared with the E-counterpart (δ 6.39-6.44).

7) The desilylation product from 3a gave ^1H NMR data in accord with the values reported for meso-1,5-hexadien-3,4-ol (4): G. Dana, J. Chuche, and M. R. Monot, Bull. Soc. Chim. Fr., 5, 3308 (1967). The anti-configulation of 3b (major) was assigned by the similarity of its ^1H NMR and ^{13}C NMR spectra to those of anti-3a. The stereochemistry of 3c was determined by its conversion, by hydrogenation and desilylation, to the known saturated alcohol (5) of which ^1H NMR spectrum shows two doublets due to the benzylic proton at δ 4.55 (J=7.5 Hz) and 4.21 (J=3.8 Hz) for the anti- and syn-isomer, respectively: C. A. Kingsbury, J. Org. Chem., 35, 1319 (1970). The stereochemistry of 3d was assigned by its conversions to the known acetonide of 1-hexyn-5-en-3,4-diol (6) of which ^1H NMR spectrum shows two sets of two singlets due to the two methyl groups at δ 1.31 and 1.49 for the major anti-isomer and at δ 1.37 and 1.43 for the syn-isomer: S. Galay and Y. Pascal, Bull. Soc. Chim. Fr., 10, 3978 (1972).



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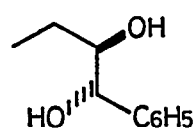

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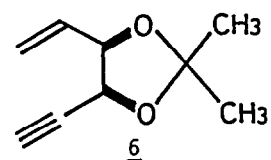

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8) K. Mikami, Y. Kimura, N. Kishi, and T. Nakai, J. Org Chem., 48, 279 (1983); K. Mikami and T. Nakai, "Physical Organic Chemistry 1986", ed. M. Kobayashi, Elsevier: London, 153 (1987).

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