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Asymmetric [2,3]-Wittig Rearrangement Induced by a Chiral Carbanion Whose Chirality Was Transferred from an Epoxide

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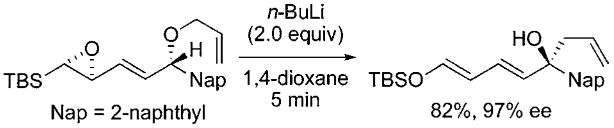
ABSTRACT



The enantioselective [2,3]-Wittig rearrangement of 1-allyloxy-1-(naphthalen-2-yl)-4-siloxy-2,4-pentadienyl anion, derived from optically enriched 4,5-epoxy-1-(naphthalen-2-yl)-5-silyl-2-pentenyl allyl ether via a base-induced ring opening of the epoxide followed by Brook rearrangement, has been studied. The chirality of the epoxide was transferred to the alcohols in up to 97% ee, depending on the solvent used. The best result was obtained in 1,4-dioxane at a temperature above room temperature.

[2,3]-Wittig rearrangement has become a powerful strategy for organic synthesis, and its asymmetric variants have been extensively explored in recent years.[1] Among these, an approach that employs a chiral nonracemic carbanion,[2] which is usually generated by enantioselective deprotonation with a chiral base[3] or a chiral ligand-bound metal reagent,[4] appears to be attractive in terms of simplicity and generality. We report here asymmetric [2,3]-Wittig rearrangement triggered by a nonracemic carbanion generated by chirality transfer from epoxide via Brook rearrangement.[5]

In our earlier work[6,7] on epoxysilane rearrangement (**1** → **5**), we showed that readily available epoxide chirality can be transferred to a carbanion via Brook rearrangement (**3** →

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(1) For reviews on [2,3]-Wittig rearrangement, see: (a) Nakai, T.; Mikami, K. *Chem. Rev.* **1986**, *86*, 885−902. (b) Marshall, J. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, pp 975−1014. (c) Mikami, K.; Nakai, T. *Synthesis* **1991**, 594−604. (d) Nakai, T.; Mikami, K. *Org. React.* **1994**, *46*, 105−209. (e) Nakai, T.; Tomooka, K. *Pure Appl. Chem.* **1997**, *696*, 595−600.

(2) (a) Verner, E. J.; Cohen, T. *J. Am. Chem. Soc.* **1992**, *114*, 375−377. (b) Hoffmann, R.; Brückner, R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 647−649. (c) Tomooka, K.; Igarashi, T.; Watanabe, M.; Nakai, T. *Tetrahedron Lett.* **1992**, *39*, 5795−5798.

(3) (a) Marshall, J. A.; Lebreton, J. *J. Am. Chem. Soc.* **1988**, *110*, 2925−2931. (b) Marshall, J. A.; Lebreton, J. *J. Org. Chem.* **1988**, *53*, 4108−4112.

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(5) For reviews on Brook rearrangement, see: (a) Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*, Wiley & Sons: New York, 2000. (b) Brook, A. G.; Bassindale, A. R. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; pp 149−221. (c) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77−84. (d) Moser, W. H. *Tetrahedron* **2001**, *57*, 2065−2084.

(6) (a) Takeda, K.; Kawanishi, E.; Sasaki, M.; Takahashi, Y.; Yamaguchi, K. *Org. Lett.* **2002**, *4*, 1511−1514. (b) Sasaki, M.; Kawanishi, E.; Nakai, Y.; Matsumoto, T.; Yamaguchi, K.; Takeda, K. *J. Org. Chem.* **2003**, *68*, 9330−9339.

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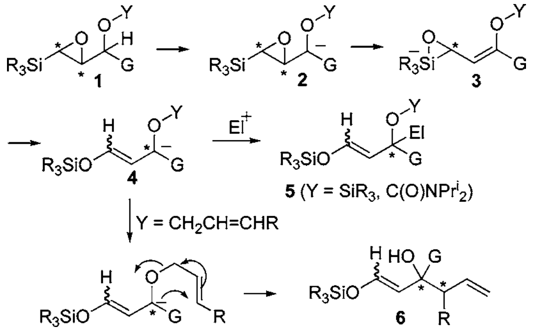
4) with a modest level of enantioselectivity and suggested that acceleration of the reaction of the carbanion with an electrophile (**4** → **5**) can suppress the racemization (Scheme 1).

Scheme 1. Brook Rearrangement-Mediated Epoxysilane Rearrangement



First, we examined tandem epoxysilane rearrangement/[2,3]-Wittig rearrangement (**1** (Y = $CH_2CH{=}CHR$) → **4** → **6**), anticipating that the chirality of epoxide would be transferred to the carbanion without racemization due to the intramolecularity of the reaction with an electrophile, and we focused on model compound **7**, which was obtained from the corresponding epoxyaldehyde.[6] Treatment of a diastereomeric mixture of **7** with a variety of bases resulted in recovery of the starting material. Since the failure of the reaction was attributed to insufficient acidity of the proton at C-1 and a sterically congested environment around the proton, we attempted to introduce a double bond between the epoxysilane moiety and the aryl substituent. Among the substrates examined, the 2-naphthyl derivatives **8a** and **8b**, which were obtained from the corresponding epoxy aldehyde,[8] provided the best results in terms of separability of diastereomers (Figure 1).

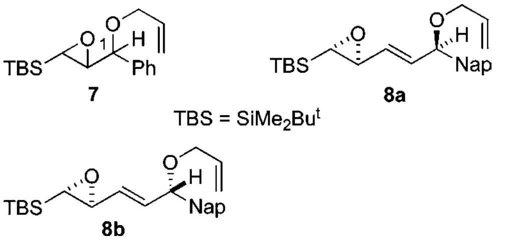
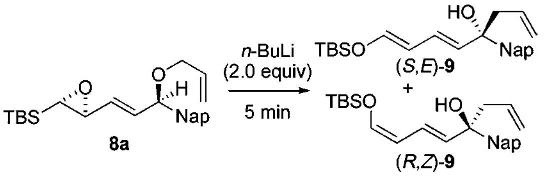


Figure 1.

When optically enriched **8a** was treated with *n*-BuLi (2.0 equiv) in THF, the most common solvent for [2,3]-Wittig rearrangement, for 5 min at −80° to −75 °C, the tandem rearrangement products (*E*)- and (*Z*)-**9** were obtained in 46% yield and in racemic form (Table 1, entry 1). Although the asymmetric induction remained poor in the solvent at higher temperatures (entry 3), change in the solvent to other ethereal solvents resulted in dramatic improvement in the asymmetric induction (entries 5−8). The use of 1,4-dioxane[9] provided excellent enantiomeric purity (entries 7 and 8).

Table 1. [2,3]-Wittig Rearrangement of **8a**



entry	solvent	temperature (°C)	yield (%)	recovered SM[a] (%)	*E*/*Z*	ee *E*	*Z* (%)[b]
1	THF	−80 to −75	46	45	5.3:1	0	0
2	THF	−35 to −30	88	−	2.4:1	0	0
3	THF	−25 to −30	80	−	1.2:1	7	0
4	Et_2O	−80 to −75	0	94	−	−	−
5	Et_2O	−35 to −30	45	35	1:9.5	81	74
6	Et_2O	−25 to −30	72	−	1:6.8	84	80
7	1,4-dioxane	−25 to −30	85	−	1:2.6	96	74
8	1,4-dioxane	−50 to −60	82	−	1:2.6	91	82

[a] SM = starting material. [b] Corrected for the ee of the starting material (90% ee).

Reaction of diastereomer **8b** proceeded in a similar manner to give (*R*,*E*)- and (*S*,*Z*)-**9**, which are enantiomeric to those obtained from **8a**, respectively (Table 2). The absolute configurations of **9** were assigned after conversion to **10**, respectively, by comparison of the chiral HPLC to the one obtained from [2,3]-Wittig rearrangement of (*S*)-**11**.[10]

It is particularly noteworthy that chirality of a carbanion derived from the epoxide, conjugated with both a naphthyl group and a double bond, can be retained even above room temperature. Although a full understanding of the actual stereochemical process must await detailed mechanistic studies, the observed stereospecificity suggests (1) the formation of a carbanion precursor in a concerted manner followed by [2,3]-Wittig rearrangement before racemization or (2) the direct formation of [2,3]-Wittig rearrangement products from a silicate derivative, a possible intermediate in the Brook rearrangement, without involvement of a carbanion intermediate.

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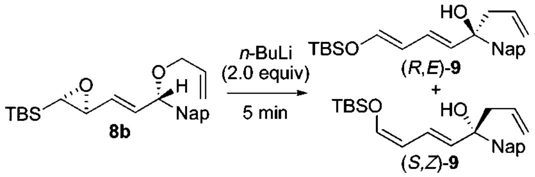
(7) Although the reaction of optically enriched **1** (Y = $SiMe_2Bu^t$, G = CN) with benzyl bromide gave **5** in completely racemic form, the change in Y to $C(O)N^iPr_2$ resulted in the formation of (*Z*)-**5** in 21% yield and 37% ee, which will be reported elsewhere. Kawanishi, E.; Takeda, K. Hiroshima University, Japan. Unpublished results.

(8) For the preparation of **8a**,**b** and determination of their absolute stereochemistries, see the Supporting Information.

(9) To the best of our knowledge, the solvent has not been used in [2,3]-Wittig rearrangement, probably because the rate of racemization of the carbanion has been thought to be much faster than that of the reaction with an electrophile at temperatures higher than its freezing point (11 °C).

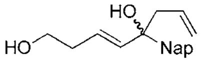
(10) (*S*)-**11** was prepared from the corresponding allyl alcohol according to the kinetic resolution procedure of Sharpless (see ref 11). On the basis of the results for [2,3]-Wittig rearrangement of (*S*)-**12** (Table 3), we deduced that [2,3]-Wittig rearrangement of (*S*)-**11** proceeds with inversion of configuration at the lithium-bearing carbon atom in the same way as reported for the alkyl counterparts (see ref 2).

Table 2. [2,3]-Wittig Rearrangement of **8b**

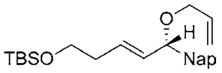


entry	solvent	temperature (°C)	yield (%)	recovered SM[a] (%)	E/Z	ee E	Z (%)[b]
1	THF	−80 to −75	54	36	*E*	0	–
2	THF	−35 to −30	91	–	*E*	0	–
3	THF	−25 to −30	90	–	15.4:1	5	0
4	Et_2O	−80 to −75	0	84	–	–	–
5	Et_2O	−35 to −30	51	41	12.0:1	90	36
6	Et_2O	−25 to −30	71	–	2.6:1	91	58
7	1,4-dioxane	−25 to −30	92	–	8.1:1	97	45
8	1,4-dioxane	−50 to −60	81	–	5.3:1	96	49

[a] SM = starting material. [b] Corrected for the ee of the starting material (91% ee).

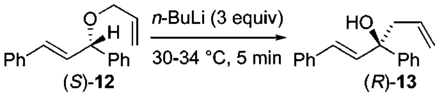


(*R*,*S*)-**10**



(*S*)-**11**

Table 3. [2,3]-Wittig Rearrangement of (*S*)-**12**



entry	solvent	additive	yield (%)	ee (%)[c]
1	THF	–	95	0
2	Et_2O	–	75	35
3	Et_2O[a]	–	39	9
4	1,4-dioxane	–	70	71
5	1,4-dioxane	HMPA	50[b]	0
6	1,3-dioxane	–	96	0

[a] *t*-BuLi was used at −80 °C. [b] 40% of (*S*)-**12** was recovered. [c] Corrected for the ee of the starting material (99% ee).

To obtain information about the configurational stability of a carbanion between an aryl group and a double bond, we decided to examine [2,3]-Wittig rearrangement of optically enriched (*S*)-**12**,[11] in which racemization may be more facile. Although no asymmetric induction was observed in THF, reactions in 1,4-dioxane were found to show the best enantioselectivity again to give (*R*)-**13** (Table 3, entries 1 and 4).[12] It is notable that less enantioselectivity was observed at a lower temperature in Et_2O (entries 2 and 3), suggesting that the loss of chirality is at least partly attributed to the racemization due to decreased rate of the [2,3]-Wittig rearrangement at a lower temperature. These results are consistent with the former possibility, although the latter possibility of tandem epoxysilane rearrangement/[2,3]-Wittig rearrangement cannot be ruled out.

The origin of the excellent enantioselectivity observed in 1,4-dioxane is unclear at present, but possibly it may be due to the decreased rate of racemization by chelation of the lithium cation with the two oxygens. This is supported by the fact that the addition of HMPA in 1,4-dioxane (entry 5) and the use of 1,3-dioxane (entry 6) resulted in complete racemization.

In summary, we have demonstrated that chirality of epoxide can be transferred to a carbanion via anion-induced ring opening followed by Brook rearrangement and that the carbanion can participate in [2,3]-Wittig rearrangement without racemization. Moreover, we have shown that vinyl-substituted benzyllithium derivatives, which have a marked tendency to racemize, are relatively stable; clearly they are sufficiently long-lived to be trapped by [2,3]-Wittig rearrangement without racemization in 1,4-dioxane at room temperature. Detailed mechanistic interpretation of the stereochemical results will be reported in a forthcoming full article.

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Supporting Information Available: Full experimental details and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] (*S*)-**12** was prepared from cinnamaldehyde by a three-step sequence: (1) PhLi, (2) kinetic resolution according to the protocol of Sharpless, and (3) $BrCH_2CH{=}CH_2$. Gao, Y.; Klunder, J. M.; Hanson, R. M.; Masamune, H.; Ko, S. Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765−5780.

[12] The absolute configuration of the major enantiomer was determined to be *R* by comparison of the chiral HPLC to the one derived from (*R*)-mandelic acid (see Supporting Information), indicating an inversion of configuration at the lithium-bearing carbon atom (according to the protocol of Sharpless, see ref 11).