

SmI₂-Induced 2,3-Wittig Rearrangement: Regioselective Generation of α -Allyloxy Carbanions via 1,5-Hydrogen Transfer of Vinyl Radicals

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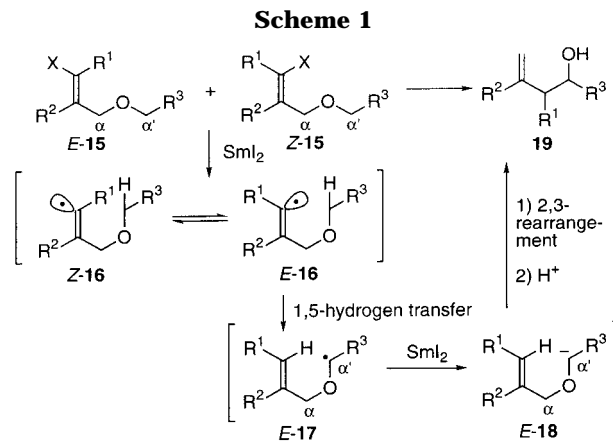
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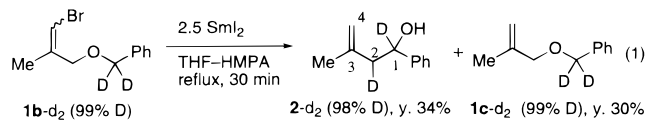
2,3-Wittig rearrangement of allyl ethers is widely used in organic synthesis.¹ Numerous studies have focused on their stereochemistry,^{1–3} but there are few methods for generating an α -allyloxy anion regioselectively and under mild reaction conditions.⁴ In this communication, we report a novel 2,3-Wittig rearrangement involving regioselective metalation at carbon α to the ethereal oxygen via 1,5-hydrogen atom transfer⁵ by the reaction of γ -haloallyl ethers with SmI₂ in benzene–HMPA.^{6,7}

Treatment of benzyl γ -iodomethyl allyl ether **1a** with 2.5 equiv of SmI₂ in benzene containing 10% HMPA under nitrogen atmosphere at room temperature for 10 min gave homoallyl alcohol **2** in 81% yield (Table 1, run 1, conditions A).⁸ The reaction also proceeded with the corresponding bromide, but a higher temperature (conditions C) or a longer reaction time (conditions D) was required (runs 3, 4). Both (*E*)- and (*Z*)-vinyl halides were found to be effective for the reaction.

Intramolecular 1,5-hydrogen atom transfer plays an important part in this reaction.⁹ As outlined in Scheme 1, a single electron transfer from SmI₂ to vinyl halides **15** generates reactive vinyl radicals **16**, which abstract a hydrogen at the α' -carbon to the ethereal oxygen via a



six-membered transition state to give α -allyloxy carbon radicals **17** followed by reduction with SmI₂ to give the corresponding carbanions **18**.^{10,11} 2,3-Sigmatropic rearrangement of the anions gives homoallyl alcohols **19**. Lower yields of the product are obtained in THF (runs 2, 5), which has α -hydrogen-donating ability, than in benzene, and this can be attributed to the competition between intermolecular hydrogen abstraction and intramolecular 1,5-hydrogen atom transfer. The hydrogen undergoing 1,5-shift should be observed at the C-2 position of the product in the proposed mechanism. Thus, we carried out the reaction by using **1b** which was 99% deuterium-labeled at the benzylic methylene as illustrated in eq 1. The ¹H NMR spectrum of the product indicated that one of the two deuteriums was present at



C-2, and the other at C-1 (both 98% D).^{12,13} On the other hand, both deuteriums were found to remain at the benzylic position (99% D) in the alkene **1c** with none at the terminal vinylic position.¹³

When unsymmetrical diallyl ethers are used as a starting compound for base-induced Wittig rearrangements, control over the regioselectivity of carbanion formation (α vs α') becomes important. Nakai and his co-workers have established that the regioselectivity of deprotonation by *n*-butyllithium depends on the difference in the total number of α - and/or γ -substituents, which exclusively depress lithiation on the allylic moiety, between the two allylic moieties.¹⁴ These results indicate the difficulty of realizing the formation of one regioisomeric carbanion, independent of the substituents, leading to the desired product with exclusion of the other *via* base-deprotonation. However, these limitations can be

(10) In order to prove the formation of an α -allyloxy carbanion, the reaction of **1a** with SmI₂ was performed in the presence of D₂O in THF–HMPA. The formation of **2** was completely depressed, and **1a** and **1c** were obtained in 53% and 25% yield, respectively. Incorporation of deuterium into the benzylic position of **1c** (56% D) was observed. No tetrahydrofuran derivative, which could be formed by radical cyclization of an α -allyloxy carbon radical, was observed.^{9b}

(11) Organosamariums have been shown to be involved in SmI₂-induced reactions, see: (a) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236–8246. (b) Curran, D. P.; Fevig, T. L.; Totleben, M. J. *Synlett* **1990**, 773–774.

(12) This result indicates that the reaction proceeds by 2,3-rearrangement, not by 1,2-rearrangement.

(13) A similar result was obtained for the reaction under conditions C.

(14) Nakai, T.; Mikami, K.; Taya, S.; Fujita, Y. *J. Am. Chem. Soc.* **1981**, *103*, 6492–6494.

[†] Kobe Gakuin University.

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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. *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 3, pp 975–1014. (c) Nakai, T.; Mikami, K. *Org. React.* **1994**, *46*, 105–210.

(2) For recent reports, see: (a) Konno, T.; Umetani, H.; Kitazume, T. *J. Org. Chem.* **1997**, *119*, 137–150. (b) Nakai, T.; Tomooka, K. *Pure Appl. Chem.* **1997**, *69*, 595–600. (c) Kress, M. H.; Yang, C.; Yasuda, N.; Grabowski, E. *Tetrahedron Lett.* **1997**, *38*, 2633–2636.

(3) (a) Mikami, K.; Kimura, Y.; Kishi, N.; Nakai, T. *J. Org. Chem.* **1983**, *48*, 279–281. (b) Tsai, D. J.; Midland, M. M. *J. Org. Chem.* **1984**, *49*, 1842–1843. (c) Goepfel, D.; Münster, I.; Brückner, R. *Tetrahedron* **1994**, *50*, 3687–3708.

(4) (a) Still, W. C.; Mitra, A. *J. Am. Chem. Soc.* **1978**, *100*, 1927–1928. (b) Broka, C. A.; Shen, T. *J. Am. Chem. Soc.* **1989**, *111*, 2981–2984. (c) Mulzer, J.; List, B. *Tetrahedron Lett.* **1996**, *37*, 2403–2404.

(5) We found that α -halovinyl radicals arising from 3-alkoxy-1,1-dihalo-1-alkenes with SmI₂ underwent 1,5-hydrogen atom transfer to give α -alkoxy radicals in competition with SET from SmI₂ to the vinyl radicals leading to the generation of alkylidenecarbenes, see: Kunishima, M.; Hioki, K.; Kato, A.; Tani, S. *Tetrahedron Lett.* **1994**, *35*, 7253–7254.

(6) (a) Kunishima, M.; Hioki, K.; Ohara, T.; Tani, S. *J. Chem. Soc., Chem. Commun.* **1992**, 219–220. (b) Kunishima, M.; Hioki, K.; Kono, K.; Sakuma, T.; Tani, S. *Chem. Pharm. Bull.* **1994**, *42*, 2190–2192.

(7) For recent reviews on SmI₂, see: (a) Molander, G. A. *Org. React.* **1994**, *46*, 211–367. (b) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307–338.

(8) Representative procedure for the reaction is as follows. **1a** (44.4 mg, 0.154 mmol) in benzene (1.5 mL) was added to a solution of SmI₂ (2.76 mL of 0.140 mol/L, 0.385 mmol) in benzene–HMPA under nitrogen at rt. After 10 min, the mixture was quenched with K₂CO₃ solution and extracted with ether. The crude product was purified by TLC (hexane:AcOEt = 8:2) to give 20.2 mg of 3-methyl-1-phenyl-3-buten-1-ol (**2**, 81%) and the hydrodeiodinated allyl ether (**1c**: X = H, 2.9 mg, 12%).

(9) (a) Murakami, M.; Hayashi, M.; Ito, Y. *J. Org. Chem.* **1992**, *57*, 793–794. (b) Capella, L.; Montecocchi, P. C.; Navacchia, M. L. *J. Org. Chem.* **1995**, *60*, 7424–7432.

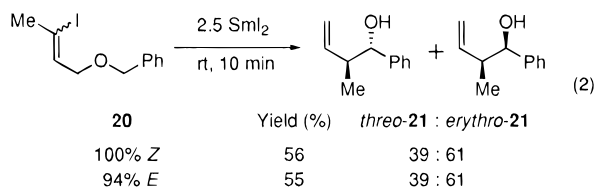
Table 1. SmI₂-Mediated 2,3-Rearrangement of γ -Halogenoallylic Ethers

Run	γ -Halogenoallylic Ether	(<i>E</i> : <i>Z</i>) ^a	Product	Conditions ^b	Yield (%) ^c	Yield (%) ^d of alkene (X = H)
1		1a: X = I (46 : 54)		A	81	1c 12
2		1a (46 : 54)		B	60 ^d	18 ^d
3		1b: X = Br (70 : 30)		C	68 ^d	15 ^d
4		1b (55 : 45)		D	78 ^d	21 ^d
5		1b (70 : 30)		E	59 ^d	22 ^d
6		3b: X = Br (45 : 55)		C	62	— ^e
7		5a: X = I (68 : 32)		A	64	— ^e
8		5b: X = Br (53 : 47)		C	51	— ^e
9		7b: X = Br (63 : 37)		C	55 ^d	— ^e
10		9a: X = I (64 : 36)		A	81	9c trace
11		9b: X = Br (69 : 31)		C	52	3
12		11b X = Br (0 : 100)		C	86	11c trace
13		13a: X = I (62 : 38)		A	63	13c 31
14		13b: X = Br (53 : 47)		C	33	5

^a Determined by NMR and/or GC. ^b A: Room temperature, 10 min in benzene–HMPA (9 : 1); B: Room temperature, 10 min in THF–HMPA (9 : 1); C: Reflux, 30 min in benzene–HMPA (9 : 1); D: Room temperature, 5 h in benzene–HMPA (9 : 1); E: Reflux, 30 min in THF–HMPA (9 : 1). ^c Isolated yield. ^d Determined by GC. ^e Not determined.

overcome by SmI₂-mediated metalation as demonstrated by runs 7–12 in Table 1. Since 1,5-hydrogen atom transfers are favored over 1,3-shifts,^{15,16} the anion can be generated regioselectively on an allyl group rather than on the γ -haloallyl group. The formation of **6** from **5** with SmI₂ indicates selective metalation on the allylic moiety possessing an unfavorable γ -substituent. The regiochemistry of carbanion formation of diallyl ethers (**7**, **9**, **11**), of which both allylic moieties have neither α - nor γ -substituents, can be controlled completely. It is noteworthy that regioisomeric products **10** and **12** could be obtained regioselectively from **9** and **11**, respectively. Metalation of alkyl allyl ether **13** takes place preferentially on the alkyl group having lower acidic α -protons leading to the formation of **14**.

We observed the reactions of benzyl crotyl ether derivatives **20** with defined stereochemistries. Interestingly, the same distribution of the products **21** from either of the geometrical isomers was observed (eq 2).¹⁷ Unfortunately, the selectivity was low in this case (*vide*



infra), but this result is very important from mechanistic viewpoint. Because of the low inversion barrier of vinyl

radicals,¹⁸ rapid isomerization between (*E*)-**16** and (*Z*)-**16** would occur, and the correlation between the geometry at **15** and **16** would be lost. The 1,5-hydrogen atom transfer is possible only for isomer (*E*)-**16**, whose half-occupied orbital can be directed to a hydrogen undergoing transfer, and, therefore, this step is responsible for the geometry of alkene **18**. Thus, the stereochemistry of **19** is not determined by the geometry of the starting vinyl halides. It has been shown that the *Z*-form of benzyl crotyl ether exhibits a high *erythro* selectivity whereas *E*-form shows a low and sometime the opposite sense of diastereoselectivity in base-deprotonation.^{1a,3a} Thus, the above result is compatible with *E*-geometry of **18** undergoing rearrangement and, therefore, also supports the reaction mechanism.

The present SmI₂-induced Wittig rearrangement proceeds in a regioselective manner under nonbasic conditions. This is the first example, to our knowledge, of a successful attempt to achieve the regioselective metalation of unsymmetrical diallyl ethers. In addition, the reaction can be effected at room temperature, and the starting γ -halovinyl ethers are more stable and accessible¹⁹ than are silyl- or stannylmethyl allyl ethers used for the Still–Wittig rearrangement.^{4a,c,20} Further detailed studies of the stereochemistry of the rearrangement and extension to more complex compounds are under investigation.

Supporting Information Available: Experimental procedures and spectral data for selected compounds (9 pages).

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(17) In the case of (*E*)- or (*Z*)-3-iodocrotyl 2-butynyl ether, the *threo*-selectivity was improved to 84:16, 90:10, respectively.

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(19) There are so many methods available for the synthesis of alkenyl halides, see: Larock, R. C. *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*; VCH: New York, 1989.

(20) Although Still-type protocols are known to exhibit a high regioselectivity, substrates utilized for reported reactions are virtually restricted to a stannylated methyl ether of allyl alcohols.¹