Pentacoordinate Organoaluminum Chemistry: Catalytic Efficiency of Me₃Al in the Epoxide Cleavage with Alkynyllithiums

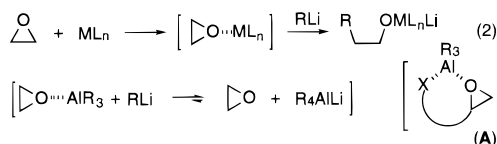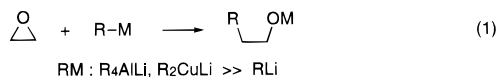**Takashi Ooi, Naoko Kagoshima, Hayato Ichikawa, and Keiji Maruoka***

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Abstract: A new and highly effective catalytic method for epoxide alkynylations has been developed that involves the chelation-controlled alkylation of heterosubstituted epoxides with Me₃Al via pentacoordinate organoaluminum complexes by taking advantage of the exceedingly high affinity of aluminum to oxygen. For example, reaction of epoxy ether, (1-benzyloxy)-3-butene oxide (**1**), in toluene with PhC≡CLi under the influence of catalytic Me₃Al (10 mol%) proceeded smoothly at 0 °C for 5 h to furnish the alkynylation product, 1-(benzyloxy)-6-phenylhex-5-yn-3-ol, in 76% yield [*cf.* 3% without Me₃Al catalyst; 78% with stoichiometric Me₃Al under similar conditions]. This represents the first catalytic procedure for the amphiphilic alkylation of epoxides. The participation of pentacoordinate Me₃Al complexes of epoxy ethers of type **1** is emphasized by comparing the reactivity with the corresponding simple epoxide, 5-phenyl-1-pentene oxide, which was not susceptible to nucleophile attack of PhC≡CLi with catalytic Me₃Al under similar conditions. The pentacoordinate complex formation of Me₃Al with epoxy ether **1** is characterized by low-temperature ¹³C and ²⁷Al NMR spectroscopy. This approach is also applicable to the selective alkynylation of tosyl aziridines with adjacent ether functionality, which provides a promising method for amino alcohol synthesis.

Introduction

The regioselective cleavage of epoxides with carbon nucleophiles is one of the most fundamental and yet important organic transformations, leading to a versatile method for the preparation of a variety of alcohols.[1] Among various organometallic reagents as carbon nucleophiles, organolithium reagents are sometimes curtailed owing to competing β-hydrogen abstractions arising from their Lewis basicity. Accordingly, these reagents are transformed to the corresponding diorganocuprates or organoaluminates to ensure a smooth epoxide opening (eq 1).[1,2] Recently, addition of BF₃·OEt₂ was reported to cause the enhancement of reactivity for the epoxide cleavage with organolithium reagents (eq 2).[3] However, this type of alkylation (*i.e.*, amphiphilic alkylation) has never been realized by combining use of highly oxygenophilic organoaluminum reagents with organolithiums because of the preferable formation of organoaluminate complexes.[2,4] In this context, we have been interested for some time in the possibility of forming chelation

$$\text{epoxide} + R-M \longrightarrow R\text{-OM} \qquad (1)$$

RM : R₄AlLi, R₂CuLi >> RLi

$$\text{epoxide} + ML_n \longrightarrow [\text{epoxide···}ML_n] \xrightarrow{RLi} R\text{-OML}_nLi \qquad (2)$$

$$[\text{epoxide···}AlR_3 + RLi \longrightarrow \text{epoxide} + R_4AlLi] \qquad (\mathbf{A})$$

complexes (**A**) of organoaluminums with certain epoxy substrates possessing adjacent heterosubstituents preferentially rather than the ate complex formation with organolithiums. We wish to report that regio- and stereocontrolled alkynylation of such heterosubstituted epoxides with alkynyllithiums can be greatly accelerated under the influence of catalytic Me₃Al (Scheme 1). This study offers the new mechanistic elucidation of the epoxide alkylation with tetraalkylaluminate complexes, which is essentially different from those of simple epoxides with aluminate complexes, and is ascribed to the intervention of unfamiliar pentacoordinate trialkylaluminum complexes (**A**) as a key intermediate.[5]

Results and Discussion

First, we chose (1-benzyloxy)-3-butene oxide (**1**) as a representative substrate for our study and examined its alkylation under various reaction conditions. Alkynylation of epoxy ether **1** in toluene with PhC≡CLi in ether proceeded quite reluctantly

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(2) Mole, T.; Jeffery, E. A. *Organoaluminum Compounds*; Elsevier: Amsterdam, 1972. (b) Negishi, E. *Organometallics in Organic Synthesis*; John Wiley & Sons: New York, 1980. (c) Zweifel, G.; Miller, J. A. *Org. React.* **1984**, *32*, 375. (d) Maruoka, K.; Yamamoto, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 668. (e) Maruoka, K.; Yamamoto, H. *Tetrahedron* **1988**, *44*, 5001.

(3) Eis, M. J.; Wrobel, J. E.; Ganem, B. *J. Am. Chem. Soc.* **1984**, *106*, 3693 and references cited therein.

(4) Recent example of organoaluminate complex as chemoselective alkynylating agent: Ahn, J. H.; Sim, T. B.; Joung, M. J.; Yoon, N. M. *Bull. Korean Chem. Soc.* **1996**, *17*, 380. For epoxide ring opening with trialkylaluminum reagents, see: Suzuki, T.; Saimoto, H.; Tomioka, H.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 3579.

(5) Ooi, T.; Kagoshima, N.; Maruoka, K. *J. Am. Chem. Soc.* **1997**, *119*, 5754. A recent impressive report on asymmetric Diels−Alder reactions describes the possibility of pentacoordinate aluminum species in their mechanistic hypothesis for asymmetric induction: Heller, D. P.; Goldberg, D. R.; Wulff, W. D. *J. Am. Chem. Soc.* **1997**, *119*, 10551. See also: Murakata, M.; Jono, T.; Mizuno, Y.; Hoshino, O. *J. Am. Chem. Soc.* **1997**, *119*, 11713. Arai, T.; Sasai, H.; Yamaguchi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **1998**, *120*, 441.

Scheme 1
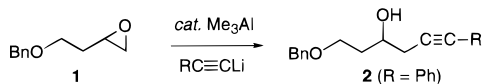
**Table 1.** Me$_3$Al-Catalyzed Alkylation of Heterosubstituted Epoxides with Alkyllithiums[a]

entry	alkyllithium (R'Li)	condition (°C, h)	yield, %[b]
1	PhC≡CLi	-78, 0.1; 0, 5	51[c] (<1)[c d]
2	PhC≡CLi	-78, 0.1; 0, 5	76, 78[e]
3	PhC≡CLi	-78, 0.1; 0, 5	70[f] (3)[d]
4	Me$_3$SiC≡CLi	-78, 0.1; 25, 5	73 (7)[d]
5	PhLi	-78, 0.1; 0, 5	59 (37)[d]
6	BuLi	-78, 0.1; 0, 5	30 (6)[d]
7	PhC≡CLi	-78, 0.1; 0, 5	76
8	Me$_3$SiC≡CLi	-78, 0.1; 0, 5	71, 45[e g]
9	PhC≡CLi	-78, 0.1; 0, 5	28
10	PhC≡CLi	-78, 0.1; 0, 5	4
11	PhC≡CLi	-78, 0.1; 0, 5	64
12	PhC≡CLi	0, 3; 25, 12	57
13	PhC≡CLi	-78, 0.1; 25, 5	55[h]

[a] Unless otherwise specified, the reaction was carried out with 1.1 equiv of alkyllithium in distilled toluene under the given reaction conditions in the presence of 10 mol % of Me$_3$Al. [b] Isolated yield. [c] Use of ether/toluene (v/v, 1:1) as solvent. [d] Isolated yield in parentheses refers to the reaction without Me$_3$Al catalyst. [e] Stoichiometric use of Me$_3$Al. [f] Use of 5 mol % of Me$_3$Al. [g] Significant amount of methylation product was contaminated. [h] 20 mol % Me$_3$Al was used.

at 0 °C to furnish only a trace amount of alkynylation product, 1-(benzyloxy)-6-phenylhex-5-yn-3-ol (**2**, R = Ph), after 5 h. Initial ate complex (PhC≡CAlMe$_3$Li) formation by mixing with PhC≡CLi and Me$_3$Al in ether/toluene (v/v, 1:1) and subsequent treatment with epoxy ether **1** under similar conditions afforded **2** in 19% yield.[4] In contrast, under the influence of catalytic

Me$_3$Al (10 mol %), reaction of **1** with PhC≡CLi in ether/toluene was accelerated to furnish **2** in higher yield (51%) at 0 °C for 5 h, indicating that the catalytic use of Me$_3$Al is indispensable in obtaining satisfactory results under these conditions. Although ether is commonly used for this type of epoxide alkylation with organoaluminates, we assumed that its property as donor solvent retards the alkylation, particularly in the presence of stoichiometric Me$_3$Al. Indeed, by switching ether/toluene solvents to toluene alone, the yields of **2** were found to be comparable with the stoichiometric or catalytic use of Me$_3$Al (78% and 76% yields, respectively) as shown in Table 1 (entry 2); this implies the involvement of the same mechanistic pathway in both the catalytic and stoichiometric systems in nonpolar solvents. It should be added that a simple epoxide, 5-phenyl-1-pentene oxide, was not susceptible to nucleophilic attack of PhC≡CLi with Me$_3$Al (10−100 mol %) under these conditions.[6] Other alkynyllithiums such as Me$_3$SiC≡CLi work equally well with Me$_3$Al catalyst (entries 4 and 8).[7] However, the present system did not seem to appreciate the use of aryllithiums and alkyllithiums as nucleophile (entries 5 and 6). The catalytic efficiency of Me$_3$Al was found to be highly dependent on how far the epoxide moiety is situated from the ethereal oxygen, which consequently manifests the importance of the proposed pentacoordinate chelate formation to attain a sufficient level of reactivity (entries 9 and 10). In addition to epoxy ether substrates, epoxy acetal is also employable and alkynylation of disubstituted epoxide appears feasible (entries 12 and 13).

The present approach has been quite useful in the selective functionalization of a bisepoxide of type **3**. Indeed, reaction of **3** with PhC≡CLi in toluene can be catalyzed by 10 mol % of Me$_3$Al to afford monoalkynylation product **4** in 68% yield, leaving the remote epoxide moiety intact as illustrated below.
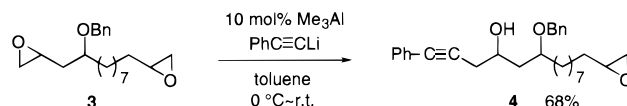

The stronger coordination of alkynyl anion than epoxy ether oxygens to an aluminum reagent normally resulted in facile ate complex formation (**B**) with Me$_3$Al in the presence of epoxy ether **1**. The key element of the present approach is the catalytic use of Me$_3$Al compared to the previously reported stoichiometric conditions in order to induce the ligand exchange between alkynyllithium and epoxy ether **1** possessing the chelating ability, thereby allowing the favorable formation of epoxy ether **1**/Me$_3$Al complex (**C**) in the presence of excess epoxy ether substrate **1** to Me$_3$Al ($n \gg 1$). Such chelation complex (**C**) is also conceivable even with the stoichiometric use ($n = 1$) of PhC≡CLi and Me$_3$Al in the nonpolar toluene solvent.
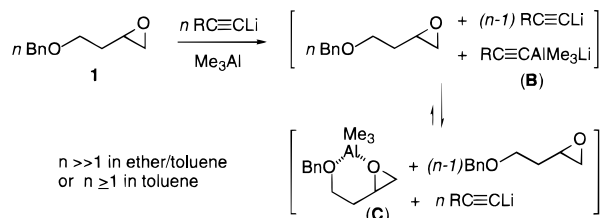
(6) The yields of the reactions were 0.7% (10 mol % of Me$_3$Al) and 4% (100 mol %), respectively.

(7) The catalytic use of Me$_3$Al is crucial for obtaining satisfactory yield of the alkynylation product in the case of Me$_3$SiC≡CLi, since a significant amount of methylation product arises from using stoichiometric Me$_3$Al (see also entry 8 of Table 1).

Scheme 2
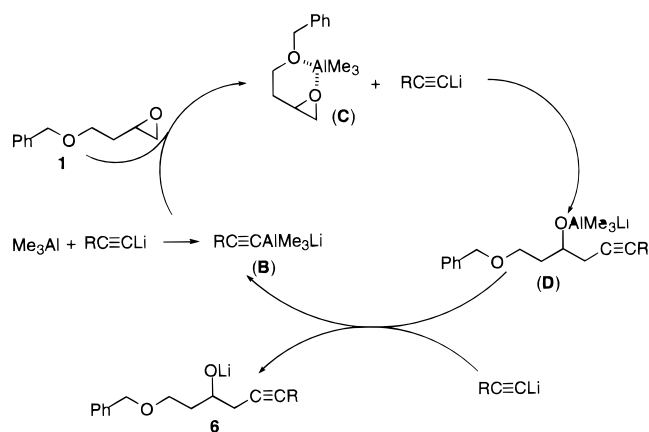
Additional evidence was obtained by low-temperature ^{13}C and ^{27}Al NMR studies of these aluminum complexes. The original signals of acyclic carbons C-1−C-4 in epoxy ether **1** occurred at δ 46.50, 49.57, 67.30, and 73.13, respectively. When **1** was complexed with Me$_3$Al in a 1:1 molar ratio in toluene-d_8 −50 °C, both a significant downfield shift of epoxide carbons and a slight upfield shift of ethereal carbons, C-1′−C-4′ in structure (**C**), were observed at δ 53.33, 58.74, 65.33, and 73.04, respectively, by ^{13}C NMR analysis at −50 °C; this suggested the expected chelate formation of aluminum with epoxy ether **1**.[8] In addition to these ^{13}C NMR data, we also carried out the low-temperature ^{27}Al NMR analysis of the complex (**C**). The original signal of Me$_3$Al appeared at δ 153 in CH$_2$Cl$_2$ at −50 °C. Addition of epoxy ether **1** to Me$_3$Al in CH$_2$Cl$_2$ showed the Al signal at δ 78, while the coordination of simple epoxide, 5-phenyl-1-pentene oxide to Me$_3$Al, caused a downfield shift to δ 167.[5] It should be noted that the Al peak of the complex of simple benzyl ether **5** with Me$_3$Al appeared at δ 155, which is close to that of the Me$_3$Al original signal. These results, together with alkynylation experiments, support the existence of pentacoordinate Me$_3$Al complex as shown in **C**.[9]
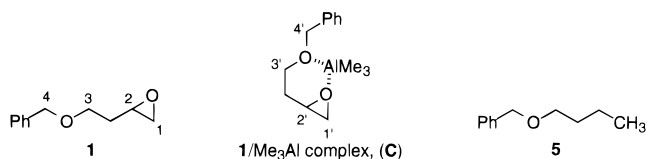

With this experimental and NMR information at hand, the present Me$_3$Al-catalyzed alkynylation of heterosubstituted epoxides can be interpreted by a mechanism as shown in Scheme 2. Thus, the ligand exchange between the initially formed RC≡CAlMe$_3$Li and epoxy ether **1** takes place to generate the pentacoordinate Me$_3$Al complex **C**. Then, RC≡CLi attacks the epoxide moiety of complex **C** at the less hindered site to give alkynylation complex **D**. Further ligand exchange of **D** with alkynyllithium produces the end product **6** with regeneration

of alkynylaluminate (**B**) for further use in the catalytic cycle of the alkynylation.[10]

Our catalytic system was successfully applicable to the alkynylation of tosyl aziridines with adjacent ether functionality,[11] which should provide a promising method for the synthesis of amino alcohols. Treatment of tosyl aziridine **7**[12] with PhC≡CLi in the presence of catalytic Me$_3$Al in toluene at 0 °C for 5 h gave rise to the corresponding alkynylation product **8** in 66% yield, while the reaction in the absence of Me$_3$Al proceeded sluggishly under similar reaction conditions (7% yield). The reaction of one carbon homologated tosyl aziridine **9**[12] with PhC≡CLi worked equally well under the influence of catalytic Me$_3$Al to furnish the homopropargyl tosylamide **10**. The control experiment with simple aziridine **11**,[12] where the addition of catalytic Me$_3$Al had almost no influence on the reaction rate, supports the proposed catalytic cycle, and its efficacy is based on the formation of the pentacoordinate organoaluminum complex.
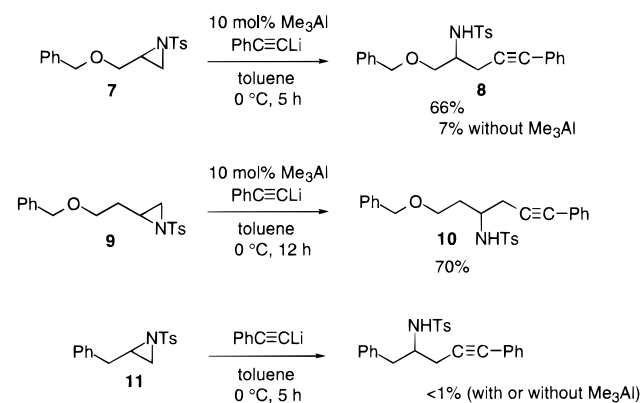
Conclusions

This study illuminates the new synthetic aspect of pentacoordinate trialkylaluminum complexes; *i.e.*, regio- and stereoselective cleavage of heterosubstituted epoxides with alkynyllithiums can be smoothly facilitated by catalytic Me$_3$Al via the pentacoordinate chelate complex formation as a key intermediate. The proposed catalytic mechanism has been considered to be operative even in the stoichiometric system in nonpolar solvents, which therefore provides new mechanistic elucidation of the epoxide alkylation with tetraalkylaluminate complexes.

Experimental Section

General. Infrared (IR) spectra were recorded on a Shimadzu FT-IR 8100A spectrometer. ^{1}H, ^{13}C, and ^{27}Al NMR spectra were measured on Varian Gemini-300 (300 MHz) and Bruker MSL-400 (400 MHz) spectrometers. Analytical gas−liquid phase chromatography-mass spectrometer (GC-MS) was performed on Shimadzu GC-17A instruments equipped with a EI-detector and a capillary column of DB-1 (J&W SCIENTIFIC, 0.25 × 30 000 mm) with helium as carrier gas,

(8) Although the upfield shift of ethereal carbons suggests the interaction of aluminum with ether oxygen, we have not yet been able to identify the origin of this behavior. We did, however, confirm the formation of the expected chelate-type complex (**C**) by ^{27}Al NMR analysis.

(9) Benn, R.; Rufinska, A. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 861. See also: (a) van Vliet, M. R. P.; Buysingh, P.; van Koten, G.; Vrieze, K.; Kojic-Prodic, B.; Spek, A. L. *Organometallics* **1985**, *4*, 1701. (b) Muller, G.; Lachmann, J.; Rufinska, A. *Organometallics* **1992**, *11*, 2970. (c) Rutherford, D.; Atwood, D. A. *Organometallics* **1996**, *15*, 4417. (d) Fryzuk, M. D.; Giesbrecht, G. R.; Olovsson, G.; Rettig, S. J. *Organometallics* **1996**, *15*, 4832.

(10) Pfaltz and Mattenberger reported that regioselective ring opening of α- and β-alkoxyepoxides with Me$_3$Al was markedly accelerated by 0.3 equiv of BuLi or MeOLi. Although the mechanistic detail was not discussed at all, ate complex formation could probably enable the facile methyl transfer in their system. We acknowledge the reviewer for bringing this information to our attention. See: Pfaltz, A.; Mattenberger, A. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 71.

(11) Review: Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599 and references cited therein.

(12) For the preparation of aziridines **7**, **9**, and **11**, see: (a) Tanner, D.; Somfai, P. *Tetrahedron* **1988**, *44*, 619. (b) Duggan, M. E.; Karanewsky, D. S. *Tetrahedron Lett.* **1983**, *24*, 2935.

(13) Zhang, H.; Fletcher, M. T.; Avery, J. W.; Kitching, W. *Tetrahedron Lett.* **1977**, *38*, 3477. (b) Jakob, B.; Voss, s G.; Gerlach, H. *Tetrahedron: Asymmetry* **1996**, *7*, 3255.

and GCMS-QP5000. All experiments were carried out under an atmosphere of dry argon. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF$_{254}$, 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel (E. Merck 9385). Microanalyses were accomplished at the Center for Instrumental Analysis, Hokkaido University. The high-resolution mass spectra (HRMS) were conducted at the School of Agriculture, Hokkaido University.

In experiments requiring dry solvents, ether, and tetrahydrofuran (THF) were purchased from Kanto Chemical Co., Ltd. as "Dehydrated". Toluene was freshly distilled from sodium metal. Benzene and hexane were dried over sodium metal. Methylene chloride and DMF were stored over 4 Å molecular sieves. Pyridine and triethylamine were stored over KOH pellets. Trimethylaluminum was obtained from Toso-Akzo Chem. Co. Ltd., Japan. Other simple chemicals were purchased and used as such.

Preparation of Epoxy Ethers. Epoxy ethers were prepared according to the following procedures: (1) conversion of olefinic alcohols to the corresponding benzyl ethers by NaH, benzy bromide in THF; (2) subsequent simple epoxidation with MCPBA in CH$_2$Cl$_2$.

Epoxy ether 1:[13] ^{1}H NMR (CDCl$_3$) δ 7.27−7.36 (5H, m, Ph), 4.54 (2H, s, PhCH$_2$O), 3.60−3.66 (2H, m, OCH$_2$), 3.05−3.12 (1H, m, CCHO), 2.79 (1H, t, J = 4.8 Hz, O-CH), 2.53 (1H, dd, J = 2.7, 4.8 Hz, O-CH), 1.87−1.96 (1H, m, CH), 1.75−1.84 (1H, m, CH).

Preparation of Epoxy Ether 3. To an ethereal solution (50 mL) of allylmagnesium bromide (24 mmol) was added 10-undecenal (3.96 mL, 20 mmol) dropwise at −78 °C under argon. The resulting mixture was stirred at −78 °C for 30 min and at 0 °C for an additional 30 min. The solution was quenched with saturated NH$_4$Cl and extracted with ether. The organic extracts were dried over Na$_2$SO$_4$. Evaporation of solvents and purification of the residual oil by column chromatography on silica gel (EtOAc/hexane = 1:9 as eluant) gave 1,13-tetradecadien-4-ol (3.54 g, 17 mmol, 84% yield) as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 5.75−5.90 (2H, m, 2(CH=C)), 4.89−5.17 (4H, m, 2(C=CH$_2$)), 3.64 (1H, brs, CHOH), 2.30 (1H, ddd, J = 4.8, 6.0, 12.6 Hz, CH), 2.14 (1H, dt, J = 8.1, 13.8 Hz, CH), 2.04 (2H, q, J = 6.9 Hz, CH$_2$), 1.61 (1H, s, OH), 1.15−1.55 (14H, m, 7CH$_2$).

After conversion to the benzyl ether with NaH and benzyl bromide in DMF at room temperature, usual epoxidation with MCPBA afforded epoxy ether **3** as a diastereomeric mixture in 28% overall yield: ^{1}H NMR (CDCl$_3$) δ 7.24−7.40 (5H, m, Ph), 4.46−4.63 (2H, m, PhCH$_2$), 3.52−3.69 (1H, m, CHOBn), 3.00−3.13 (1H, m, CCH-O), 2.88−2.94 (1H, m, CCH-O), 2.72−2.84 (2H, m, CH-O), 2.42−2.52 (2H, m, CH-O), 1.20−1.88 (18H, m, 9CH$_2$); IR (liquid film) 3042, 2930, 2856, 1497, 1456, 1352, 1259, 1094, 1069, 1028, 916, 833, 737, 698 cm^{-1}. MS: m/z 332 (M$^+$), 315, 281, 207, 177, 91 (100). Anal. Calcd for C$_{21}$H$_{32}$O$_3$: C, 75.86; H, 9.70. Found: C, 75.59; H, 9.70.

Epoxy ether 12:[14] ^{1}H NMR (CDCl$_3$) δ 7.28−7.37 (5H, m, Ph), 4.63 (1H, d, J = 12.0 Hz, PhCHO), 4.56 (1H, d, J = 12.0 Hz, PhCHO), 3.78 (1H, dd, J = 3.0, 11.4 Hz, O-CH), 3.44 (1H, dd, J = 5.7, 11.4 Hz, O-CH), 3.17-3.22 (1H, m, CCHO), 2.81 (1H, dd, J = 3.9, 4.8 Hz, O-CH), 2.63 (1H, dd, J = 2.4, 4.8 Hz, O-CH).

Epoxy ether 13:[15] ^{1}H NMR (CDCl$_3$) δ 7.19−7.41 (5H, m, Ph), 4.51 (2H, s, PhCH$_2$), 3.44−3.58 (2H, m, CH$_2$), 2.89−2.97 (1H, m, CH-O), 2.74 (1H, dd, J = 3.9, 5.1 Hz, O-CH), 2.47 (1H, dd, J = 2.7, 5.1 Hz, O-CH), 1.52−1.86 (4H, m, 2CH$_2$).

Epoxy ether 14:[16] ^{1}H NMR (CDCl$_3$) δ 7.23−7.42 (5H, m, Ph), 4.50 (2H, s, PhCH$_2$), 3.49 (2H, t, J = 6.3 Hz, CH$_2$), 2.86−2.94 (1H, m, CH-O), 2.74 (1H, dd, J = 4.2, 5.1 Hz, O-CH), 2.46 (1H, dd, J = 2.7, 5.1 Hz, O-CH), 1.45−1.75 (6H, m, 3CH$_2$).

Preparation of Epoxy Ether 15.[17] To a mixture of Me$_3$SiOTf (159 μL, 0.8 mmol) and allyltrimethylsilane (1.41 mL, 8.8 mmol) in dry

CH$_2$Cl$_2$ (25 mL) was added dropwise 2-methoxytetrahydropyrane (985 μL, 8 mmol) at −40 °C under argon. The resulting mixture was kept at −40 °C for 4 h and 0 °C for 2.5 h with stirring, and then poured into saturated NaHCO$_3$. The extractive workup was performed with ether. The ethereal extracts were washed with brine, dried over Na$_2$-SO$_4$, and concentrated. Purification of the residual oil by column chromatography on silica gel (ether/hexane = 1:20 as eluant) gave 2-(2-propenyl)tetrahydropyrane (541 mg, 4.3 mmol, 54% yield). Subsequent exposure to the usual epoxidation conditions afforded epoxide **15** in 54% yield. ^{1}H NMR (CDCl$_3$) δ 3.96−4.01 (1H, m, O-CH), 3.40−3.56 (2H, m, O-CH$_2$), 3.03−3.12 (1H, m, CCH-O), 2.75−2.82 (1H, m, O-CH), 2.48−2.51 (1H, m, O-CH), 1.74−1.87 (2H, m, CH$_2$), 1.26−1.67 (6H, m, 3CH$_2$).

Preparation of Epoxy Acetal 16. A mixture of 3-butenal diethylacetal (175 μL, 1 mmol), benzyl alcohol (310 μL, 3 mmol), and pyridinium *p*-toluenesulfonate (catalytic amount) in benzene was refluxed for 4.5 h with azeotropic removal of ethanol. The resulting solution was cooled down to room temperature and solvents were evaporated. Purification of the residual products by column chromatography on silica gel (EtOAc/hexane = 1:20 as eluant) gave 3-butenal dibenzylacetal (187 mg, 0.698 mmol, 70% yield). Simple epoxidation of the acetal with MCPBA afforded epoxy acetal **16** in 55% yield. ^{1}H NMR (CDCl$_3$) δ 7.26−7.37 (10H, m, 2Ph), 4.97 (1H, dd, J = 4.8, 6.6 Hz, CH(OBn)$_2$), 4.57−4.75 (4H, m, 2PhCH$_2$), 3.04−3.10 (1H, m, CCH-O), 2.78 (1H, t, J = 4.5 Hz, O-CH), 2.51 (1H, dd, J = 2.7, 4.8 Hz, O-CH), 2.06 (1H, ddd, J = 4.5, 6.6, 14.1 Hz, CH), 1.91 (1H, ddd, J = 4.8, 6.6, 14.1 Hz, CH); IR (liquid film) 3063, 3032, 2926, 2834, 1497, 1454, 1350, 1223, 1080, 1049, 1026, 850, 737, 698 cm^{-1}. Anal. Calcd for C$_{18}$H$_{20}$O$_3$: C, 76.03; H, 7.09. Found: C, 75.83; H, 7.10.

Epoxy ether 17:[18] ^{1}H NMR (CDCl$_3$) δ 7.25−7.35 (10H, m, 2Ph), 4.62 (2H, d, J = 12.0 Hz, PhCHO), 4.51 (2H, d, J = 12.0 Hz, PhCHO), 3.69 (2H, dd, J = 3.6, 11.4 Hz, BnO-CH), 3.53 (2H, dd, J = 6.3, 11.4 Hz, BnO-CH), 3.24−3.29 (2H, m, 2(CH-O)).

Tosyl aziridine 7:[12] ^{1}H NMR (CDCl$_3$) δ 7.85 (2H, d, J = 8 Hz, Ph), 7.27−7.34 (5H, m, Ph), 7.19−7.22 (2H, m, Ph), 4.43 (2H, s, PhCH$_2$O), 3.62 (1H, dd, J = 4.2, 11.4 Hz, OCH), 3.42 (1H, dd, J = 6.3, 11.4 Hz, OCH), 2.99−3.07 (1H, m, CH-N), 2.68 (1H, d, J = 7.2 Hz, N-CH), 2.43 (3H, s, ArCH$_3$), 2.20 (1H, d, J = 4.5 Hz, N-CH); IR (liquid film) 3011, 2926, 2866, 1599, 1497, 1454, 1326, 1160, 1097, 924, 870, 816 cm^{-1}. MS: m/z 317 (M$^+$), 212, 211, 162, 155, 147, 120, 91 (100), 65, 56. HRMS Calcd for C$_{17}$H$_{19}$NO$_3$S: 317.1087 (M$^+$). Found: 317.1106 (M$^+$).

Preparation of Tosyl Aziridine 9.[12] To a solution of epoxide **1** (1.41 g, 7.9 mmol) in 10% H$_2$O−EtOH (30 mL) was added NH$_4$Cl (854 g, 15.8 mmol) and NaN$_3$ (2.62 g, 39.5 mmol) at room temperature. The reaction mixture was heated and refluxed for 1 h. The resulting solution was poured into saturated NH$_4$Cl and extracted with ether. The ethereal extracts were dried over Na$_2$SO$_4$ and concentrated. Purification of the residual oil by column chromatography on silica gel (EtOAc/hexane = 1:4 as eluant) gave the corresponding azide (1.61 g, 7.9 mmol) quantitatively as a colorless oil. ^{1}H NMR (CDCl$_3$) δ 7.27−7.39 (5H, m, Ph), 4.52 (2H, s, PhCH$_2$), 3.94−4.07 (1H, m, CHOH), 3.59−3.77 (2H, m, CH$_2$OBn), 3.22−3.35 (2H, m, CH$_2$N$_3$), 3.16 (1H, s, OH), 1.67−1.91 (2H, m, CH$_2$).

LiAlH$_4$ (293 mg, 7.1 mmol) was added portionwise to a solution of the azide (1.61 g, 7.3 mmol) in ether (15 mL) at 0 °C under argon and the mixture was stirred there for 1 h. After the addition of H$_2$O (430 μL, 23.7 mmol) and NaF (1.33 g, 31.6 mmol), vigorous stirring was maintained at 0 °C for 30 min. The resulting mixture was filtered through celite pad and the filtrate was concentrated to give crude amino alcohol as a colorless oil (984 mg, 5.0 mmol) in 69% yield: ^{1}H NMR (CDCl$_3$) δ 7.25−7.40 (5H, m, Ph), 4.52 (2H, s, PhCH$_2$), 3.67 (2H, q, J = 6.0 Hz, CH$_2$OBn), 3.60−3.77 (1H, m, CHOH), 2.77 (1H, dd, J = 3.6, 12.6 Hz, CH-N), 2.60 (1H, dd, J = 7.8, 12.6 Hz, CH-N), 2.45 (3H, brs, OH and NH$_2$), 1.70−1.78 (2H, m, CH$_2$).

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The crude amino alcohol (983 mg, 5.0 mmol) obtained above was dissolved into pyridine (10 mL) and tosyl chloride (1.43 g, 7.5 mmol) was added at 0 °C under argon. The reaction mixture was stirred at room temperature for 7 h. This was then poured into saturated NaHCO₃ and extracted with ether. The organic extracts were dried over Na₂-SO₄. Evaporation of solvents and purification by column chromatography on silica gel (EtOAc/hexane = 1:1 as eluant) afforded hydroxy tosylamide as an orange crystal (1.26 g, 3.6 mmol) in 72% yield: ¹H NMR (CDCl₃) δ 7.72 (2H, d, J = 8.4 Hz, Ts), 7.26−7.37 (9H, m, Ts and Ph), 5.14 (1H, t, J = 6.6 Hz, NH), 4.48 (2H, s, PhCH₂), 3.85−3.96 (1H, m, CHOH), 3.55−3.72 (2H, m, CH₂OBn), 3.34 (1H, s, OH), 2.98−3.11 (1H, m, CH-N), 2.80−2.91 (1H, m, CH-N), 2.41 (3H, s, ArCH₃), 1.63−1.87 (2H, m, CH₂).

To a solution of the tosylamide (990 mg, 2.8 mmol) in THF (14 mL) was added a 1.59 M hexane solution of BuLi (3.56 mL, 5.66 mmol) at 0 °C followed by the addition of tosyl chloride (648 mg, 3.40 mmol). The mixture was then allowed to warm to room temperature and stirred there for 1 h. The solution was poured into water and extracted with ether. The ethereal extracts were dried over Na₂SO₄ and concentrated. The residual oil was purified by column chromatography on silica gel (ether/hexane/dichloromethane = 1:8:8 as eluant) to give the desired tosyl aziridine **9** as a colorless oil (728 mg, 2.2 mmol) in 78% yield: ¹H NMR (CDCl₃) δ 7.82 (2H, d, J = 8.7 Hz, Ts), 7.19−7.41 (7H, m, Ts and Ph), 4.37 (2H, s, PhCH₂), 3.41−3.48 (1H, m, CHOBn), 3.29−3.66 (1H, m, CHOBn), 2.87−2.95 (1H, m, CH-N), 2.68 (1H, d, J = 6.9 Hz, N-CH), 2.44 (3H, s, ArCH₃), 2.13 (1H, d, J = 4.5 Hz, N-CH), 1.87−1.98 (1H, m, CH), 1.51−1.62 (1H, m, CH). IR (liquid film) 3030, 2924, 2864, 1597, 1454, 1325, 1163, 1096, 930, 818, 716, 698 cm⁻¹. MS: m/z 331 (M⁺), 305, 281, 184, 44 (100). Anal. Calcd for C₁₈H₂₁-NO₃S: C, 65.23; H, 6.39; N, 4.23. Found: C, 65.05; H, 6.43; N, 4.16.

General Method of Me₃Al-Catalyzed Cleavage of Epoxide with Alkynyllithiums. To a solution of phenylacetylene (54 μL, 0.48 mmol) in freshly distilled toluene (4 mL) was added a 1.56 M hexane solution of BuLi (282 μL, 0.44 mmol) dropwise at 0 °C under argon. The suspension was stirred for 30 min and then cooled to −78 °C. Epoxy ether (0.4 mmol) was added dropwise followed by the addition of a 0.5 M hexane solution of Me₃Al (80 μL, 0.04 mmol) at the same temperature. The resulting mixture was allowed to warm to 0 °C and stirred there for 5 h. The solution was then poured into 1 N HCl and extractive workup was performed with ether. The combined organic extracts were washed with brine and dried over Na₂SO₄. Evaporation of solvents and purification of the residual oil by column chromatography on silica gel (ether/hexane as eluant) gave the corresponding homopropargyl alcohol.

Homopropargyl alcohol 2 (R = Ph): ¹H NMR (CDCl₃) δ 7.25−7.41 (10H, m, 2Ph), 4.54 (2H, s, PhCH₂O), 4.01−4.11 (1H, m, CHOH), 3.66−3.81 (2H, m, OCH₂), 3.10 (1H, d, J = 3.6 Hz, OH), 2.67 (1H, dd, J = 6.0, 16.8 Hz, CHC≡C), 2.60 (1H, dd, J = 6.3, 16.8 Hz, CHC≡C), 1.85−2.05 (2H, m, CH₂); IR (liquid film) 3451, 3032, 2920, 2884, 1491, 1454, 1364, 1099, 1028, 756, 692 cm⁻¹. Anal. Calcd for C₁₉H₂₀O₂: C, 81.40; H, 7.19. Found: C, 81.41; H, 7.25.

Homopropargyl alcohol 2 (R = SiMe₃): ¹H NMR (CDCl₃) δ 7.29−7.38 (5H, m, Ph), 4.53 (2H, s, PhCH₂O), 3.92−4.02 (1H, m, CHOH), 3.63−3.78 (2H, m, OCH₂), 3.01 (1H, d, J = 3.6 Hz, OH), 2.48 (1H, dd, J = 6.0, 16.8 Hz, CHC≡C), 2.41 (1H, dd, J = 6.3, 16.8 Hz, CHC≡C), 1.77−1.97 (2H, m, CH₂), 0.15 (9H, s, 3CH₃); IR (liquid film) 3443, 3032, 2959, 2862, 2176, 1454, 1420, 1364, 1250, 1099, 1030, 843, 760, 698, 648 cm⁻¹. Anal. Calcd for C₁₆H₂₄O₂Si: C, 69.51; H, 8.75. Found: C, 69.71; H, 8.85.

Homopropargyl alcohol 4: ¹H NMR (CDCl₃) δ 7.26−7.42 (10H, m, 2Ph), 4.44−4.67 (2H, m, PhCH₂), 4.05−4.09 (0.2H, m, CHOH), 3.90−4.03 (0.8H, m, CHOH), 3.64−3.81 (1H, m, CHOBn), 3.71 (1H, s, OH), 3.08−3.11 (0.2H, m, CCHO), 2.87−2.92 (0.8H, m, CCHO), 2.72−2.76 (0.8H, m, CH-O), 2.63−2.68 (0.2H, m, CH-O), 2.44−2.63 (3H, m, CH₂C≡C and CH-O), 2.46 (1H, dd, J = 2.4, 2.7 Hz, CH-O), 1.20−1.95 (18H, m, 9CH₂); IR (liquid film) 3489, 3034, 2930, 2856, 1491, 1456, 1094, 1074, 1028, 758, 694 cm⁻¹. MS: m/z 434 (M⁺), 391, 369, 301, 43 (100). Anal. Calcd for C₂₉H₃₈O₃: C, 80.14; H, 8.81. Found: C, 79.88; H, 8.92. After debenzylation, the diol can be converted to its acetonide, which confirms the regiochemistry of the selective alkynylation.

Homopropargyl alcohol 18 (R′ = C≡CPh): ¹H NMR (CDCl₃) δ 7.26−7.40 (10H, m, 2Ph), 4.60 (2H, s, PhCH₂O), 4.01−4.10 (1H, m, CHOH), 3.69 (1H, dd, J = 3.9, 9.6 Hz, OCH), 3.58 (1H, dd, J = 6.6, 9.6 Hz, OCH), 2.72 (1H, dd, J = 6.3, 16.8 Hz, CHC≡C), 2.66 (1H, dd, J = 6.6, 16.8 Hz, CHC≡C), 2.48 (1H, d, J = 4.8 Hz, OH); IR (liquid film) 3433, 3063, 3032, 2910, 2804, 1599, 1491, 1454, 1117, 1028, 756, 692 cm⁻¹. Anal. Calcd for C₁₈H₁₈O₂: C, 81.17; H, 6.81. Found: C, 81.21; H, 6.91.

Homopropargyl alcohol 18 (R′ = C≡CSiMe₃): ¹H NMR (CDCl₃) δ 7.27−7.42 (5H, m, Ph), 4.58 (2H, s, PhCH₂O), 3.92−4.00 (1H, m, CHOH), 3.61 (1H, dd, J = 3.9, 9.6 Hz, OCH), 3.50 (1H, dd, J = 6.6, 9.6 Hz, OCH), 2.53 (1H, dd, J = 6.0, 16.8 Hz, CHC≡C), 2.46 (1H, dd, J = 6.6, 16.8 Hz, CHC≡C), 2.39 (1H, d, J = 4.8 Hz, OH), 0.14 (9H, s, 3CH₃); IR (liquid film) 3443, 2959, 2901, 2864, 2176, 1454, 1250, 1117, 1030, 843, 760, 698 cm⁻¹. Anal. Calcd for C₁₅H₂₂OSi: C, 68.65; H, 8.45. Found: C, 68.62; H, 8.40.

Homopropargyl alcohol 19: ¹H NMR (CDCl₃) δ 7.24−7.44 (5H, m, Ph), 4.53 (2H, s, PhCH₂), 3.80−3.90 (1H, m, CHOH), 3.52−3.56 (2H, m, CH₂OBn), 2.76 (1H, brs, OH), 2.61 (2H, dd, J = 1.2, 3.0 Hz, CH₂C≡C), 1.74−1.86 (2H, m, CH₂), 1.60−1.70 (2H, m, CH₂); IR (liquid film) 3416, 3063, 3030, 2922, 2860, 2363, 1599, 1491, 1454, 1364, 1097, 1072, 1028, 758, 737, 694 cm⁻¹. MS: m/z 294 (M⁺), 276, 257, 247, 233, 220, 91 (100). Anal. Calcd for C₂₀H₂₂O₂: C, 81.60; H, 7.53. Found: C, 81.41; H, 7.69.

Homopropargyl alcohol 20: ¹H NMR (CDCl₃) δ 7.24−7.45 (5H, m, Ph), 4.51 (2H, s, PhCH₂), 3.80−3.86 (1H, m, CHOH), 3.50 (2H, t, J = 6.3 Hz, OCH₂), 2.65 (1H, dd, J = 5.0, 16.8 Hz, CHC≡C), 2.55 (1H, dd, J = 6.8, 16.8 Hz, CHC≡C), 2.02 (1H, brs, OH), 1.55−1.70 (4H, m, 2CH₂); IR (liquid film) 3417, 3063, 3030, 2937, 2862, 1599, 1491, 1454, 1362, 1101, 1028, 758, 737, 694 cm⁻¹. MS: m/z 308 (M⁺), 290, 261, 247, 231, 205, 91 (100). Anal. Calcd for C₂₁H₂₄O₂: C, 81.78; H, 7.84. Found: C, 81.77; H, 7.94.

Homopropargyl alcohol 21: The complete structural assignment has been performed after conversion to the corresponding acetate. ¹H NMR (CDCl₃) δ 7.38−7.42 (2H, m, Ph), 7.27−7.30 (3H, m, Ph), 5.16−5.25 (1H, m, CH-OAc), 3.92−3.98 (1H, m, CH-O), 3.32−3.43 (2H, m, O-CH₂), 2.63−2.83 (2H, m, CH₂C≡C), 2.08 and 2.09 (3H, s, COCH₃), 1.78−2.00 (3H, m, CH₂ and CH), 1.46−1.67 (4H, m, 2CH₂), 1.26−1.35 (1H, m, CH); IR (liquid film) 2936, 2847, 1732, 1491, 1441, 1373, 1244, 1092, 1047, 1030, 758, 692 cm⁻¹. Anal. Calcd for C₁₈H₂₂O₃: C, 75.50; H, 7.74. Found: C, 75.04; H, 7.77.

Homopropargyl alcohol 22: ¹H NMR (CDCl₃) δ 7.26−7.41 (15H, m, 3Ph), 5.02 (1H, t, J = 5.4 Hz, CH(OBn)₂), 4.74 (1H, d, J = 11.7 Hz, PhCH), 4.72 (1H, d, J = 11.7 Hz, PhCH), 4.62 (1H, d, J = 11.7 Hz, PhCH), 4.60 (1H, d, J = 11.7 Hz, PhCH), 4.04−4.13 (1H, m, CHOH), 3.00 (1H, d, J = 3.3 Hz, OH), 2.65 (1H, dd, J = 5.4, 16.5, Hz, CHC≡C), 2.58 (1H, dd, J = 6.6, 16.5 Hz, CHC≡C), 2.16 (1H, ddd, J = 2.7, 5.4, 14.1 Hz, CH), 2.03 (1H, ddd, J = 5.4, 9.3, 14.1 Hz, CH); IR (liquid film) 3446, 3032, 2929, 1491, 1456, 1207, 1126, 1057, 1026, 756, 737, 695 cm⁻¹. Anal. Calcd for C₂₆H₂₆O₃: C, 80.80; H, 6.78. Found: C, 80.75; H, 6.92.

Homopropargyl alcohol 23: ¹H NMR (CDCl₃) δ 7.29−7.39 (15H, m, 3Ph), 4.54−4.64 (4H, m, 2PhCH₂O), 4.16 (1H, dq, J = 3.0, 6.0 Hz, CH-OH), 3.83 (1H, dd, J = 7.8, 9.3 Hz, OCH), 3.75 (1H, dd, J = 5.4, 9.3 Hz, OCH), 3.69 (1H, dd, J = 6.3, 9.3 Hz, OCH), 3.65 (1H, dd, J = 5.7, 9.3 Hz, OCH), 3.17 (1H, ddd, J = 3.0, 5.4, 7.8 Hz, CH-C≡C), 2.60 (1H, d, J = 6.0 Hz, OH); IR (liquid film) 3452, 3063, 3030, 2914, 2864, 2361, 2341, 1599, 1491, 1454, 1364, 1207, 1101, 1028, 912, 758, 739, 696 cm⁻¹. MS: m/z 386 (M⁺), 311, 236, 128, 105, 91 (100). HRMS Calcd for C₂₆H₂₆O₃: 386.1883 (M⁺). Found: 386.1900 (M⁺).

Tosylamide 8: ¹H NMR (CDCl₃) δ 7.75 (2H, d, J = 8.4 Hz, Ts), 7.21−7.34 (12H, m, Ts and Ph), 5.01 (1H, d, J = 7.8 Hz, NH), 4.45 (2H, s, PhCH₂), 3.56−3.66 (2H, m, OCH and CH-N), 3.41−3.45 (1H, m, OCH), 2.72 (1H, dd, J = 5.1, 16.8 Hz, CHC≡C), 2.62 (1H, dd, J = 7.2, 16.8 Hz, CHC≡C), 2.39 (3H, s, ArCH₃); IR (liquid film) 3375, 3033, 2924, 2868, 1599, 1491, 1414, 1339, 1161, 1090, 814 cm⁻¹. MS: m/z 419 (M⁺), 344, 304, 155, 115, 91 (100), 65. HRMS Calcd for C₂₅H₂₅NO₃S: 419.1557 (M⁺). Found: 419.1570 (M⁺).

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Tosylamide 10: ^{1}H NMR (CDCl$_3$) δ 7.76 (2H, d, J = 8.4 Hz, Ts), 7.26−7.39 (12H, m, Ts and Ph), 5.36 (1H, d, J = 7.8 Hz, NH), 4.40 (2H, s, PhCH$_2$), 3.51−3.68 (2H, m, CHOBn and CHNTs), 3.41−3.49 (1H, m, CHOBn), 2.67 (1H, dd, J = 3.9, 17.1 Hz, CHC≡C), 2.53 (1H, dd, J = 7.1, 17.1 Hz, CHC≡C), 2.40 (3H, s, ArCH$_3$), 1.89 (2H, q, J = 6.0 Hz, CH$_2$); IR (liquid film) 3281, 2922, 2872, 2247, 1599, 1491, 1454, 1329, 1168, 1094, 912, 816, 758, 735, 694, 667 cm^{-1}. MS: m/z 433 (M$^+$), 363, 322, 279, 212, 43 (100). Anal. Calcd for C$_{26}$H$_{27}$NO$_3$S: C, 72.03; H, 6.28; N, 3.23. Found: C, 71.49; H, 6.43; N, 3.13.

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