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Nitrile Anion Cyclization with Epoxysilanes Followed by Brook Rearrangement/Ring-Opening of Cyclopropane Nitriles/Alkylation

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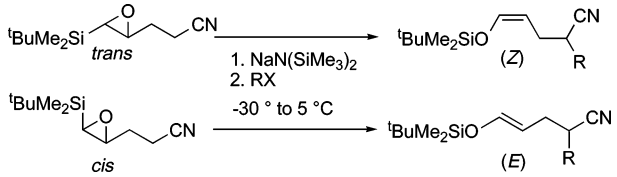
Received September 16, 2005



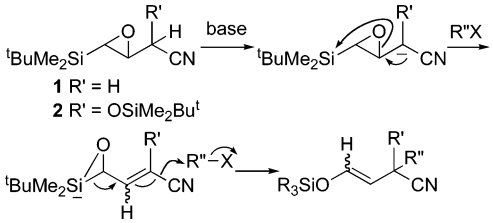
The reaction of δ-silyl-γ,δ-epoxypentanenitrile derivatives **9**−**12** with a base and an alkylating agent affords (*Z*)-δ-siloxy-γ,δ-unsaturated pentanenitrile derivatives via a tandem process that involves the formation of a cyclopropane derivative by epoxy nitrile cyclization followed by Brook rearrangement and an anion-induced cleavage of the cyclopropane ring. Exclusive formation of a (Z)-derivative from *trans*-epoxides is explained by the reaction pathway that involves a backside displacement of the epoxide by the α-nitrile carbanion and the O−Si bond formation followed by concerted processes involving Brook rearrangement and the anti-mode of eliminative ring fission of the cyclopropane from the rotamer **19**. The fact that (*E*)-isomers are exclusively obtained from *cis*-epoxides and α-cyclopropyl-α-silylcarbinol derivative **26** provides experimental support for the proposed pathway.

Introduction

Since the pioneering studies of Stork,[1] there has been great interest in epoxy nitrile cyclization,[2] which was recently further enhanced because of the ready availability of enantiomerically pure epoxides. The main reason that nitrile anions have been used extensively in synthesis is their high thermal stability and small steric demand.[2] We have recently found that γ-silyl-β,γ-epoxybutanenitrile derivatives **1** and **2** can serve as functionalized nitrile carbanion equivalents via a tandem sequence that involves a base-promoted ring opening, Brook rearrangement,[3] and alkylation of the resulting allylic anion (Scheme 1).[4]

The finding that the reaction is completed within 1 min even at −80 °C, which may be attributed to the ring strain of the epoxide, concomitant formation of an Si−O bond, and enhanced reactivity of the allylic anion with the β-siloxy group, prompted us to investigate similar reactions for a substrate in which one more carbon atom is introduced between the epoxide and the nitrile group in **1**. Reaction of epoxy nitrile derivative **3** with a base would afford **7** via a tandem process that involves the formation of cyclopropane derivative **5** by epoxy nitrile cyclization followed by Brook rearrangement and an anion-induced cleavage of the cyclopropane ring.

SCHEME 1. Tandem Base-Promoted Ring-Opening/Brook Rearrangement/Allylic Alkylation of γ-Silyl-β,γ-epoxybutanenitriles



In this case, the nucleophilic characters of the α-nitrile carbanions **4** and **6** might be critical factors in controlling the reaction. In contrast to the case of **1**, in which a base-promoted ring-opening proceeds in a concerted process

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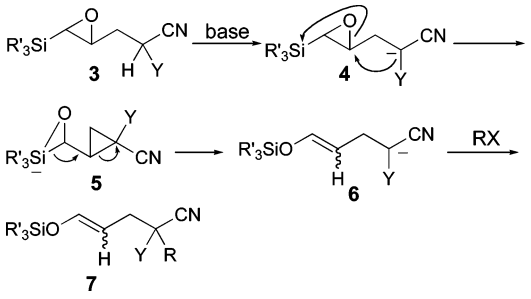
(1) (a) Stork, G.; Cama, L. D.; Coulson, D. R. *J. Am. Chem. Soc.* **1974**, *96*, 5268−5270. (b) Stork, G.; Cohen, J. F. *J. Am. Chem. Soc.* **1974**, *96*, 5270−5272.

(2) (a) Fleming, F. F.; Shook, B. C. *Tetrahedron* **2002**, *58*, 1−23. (b) Arseniyadis, S.; Kyler, K. S.; Watt, D. S. *Org. React.* **1984**, *31*, 1−364. (c) Yamamoto, M.; Yoshitake, M.; Kishikawa, K.; Kohmoto, S. *J. Synth. Org. Chem., Jpn.* **1992**, *50*, 638−651.

10.1021/jo0519413 CCC: $30.25 © 2005 American Chemical Society
Published on Web 11/10/2005

SCHEME 2. Nitrile Anion Cyclization with Epoxysilanes Followed by Brook Rearrangement/ Ring Opening of Cyclopropane Nitriles/Alkylation



via an anti-opening of the epoxide followed by the formation of an O−Si bond,[4b] the three processes, cyclopropane formation from **4** (**4** → **5**), carbanion-mediated ring-opening of the cyclopropane (**5** → **6**),[5] and alkylation (**6** → **7**), should be affected more by the nature of the carbanions. Thus, the ring-opening of the epoxide and the alkylation can be facilitated by increasing the nucleophilicity of the carbanions, whereas the cyclopropane ring cleavage can be enhanced by increasing the stability of the anion in **6**. Corbel and Durst reported that reaction of epoxy nitrile derivatives (Y = H, Ph) lacking the silyl group in **3** with LDA afforded the corresponding cyclopropane derivatives in 59% and 94% yields, respectively.[6] Stirling and co-workers also reported carbanion-activated eliminative ring fissions of cylopropanes in which the leaving group is stabilized by a cyano group, a reaction corresponding to the process from **5** to **6**.[7] With the above consideration in mind, we chose compounds **9**−**12** (Scheme 3) as substrates, in which generated α-nitrile carbanions should have different stabilities in the decreasing order of **10**, **11**, **12**,[8] and **9**. In this paper we describe in detail the reaction communicated earlier in a preliminary form.[9]

Results and Discussion

δ-Silyl-γ,δ-epoxy nitriles **9**−**12** were prepared from allyl alcohol **8** via allylation of the corresponding α-lithio

SCHEME 3. Preparation of Epoxynitriles 9−12

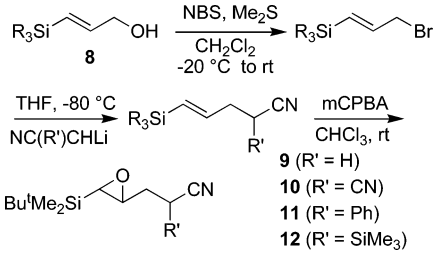
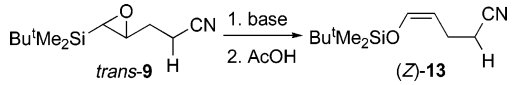


TABLE 1. Base-Mediated Isomerization of *trans*-9



base	solvent	temp (°C)	yield (%)
LDA (4 equiv)	THF	−30 to 0	
KHMDS (4 equiv)	THF	−30 to 0	25
KHMDS (4 equiv)	toluene	−30 to 0	18
KHMDS (4 equiv)	Et_2O	−30 to 0	20
NHMDS (4 equiv)	THF	−30 to 5	58
NHMDS (2 equiv)	THF	−30 to 5	73

derivatives[10] (Scheme 3). In the case of **10**, dialkylation was a major side reaction in the alkylation step of lithiomalononitrile.

First, exploratory experiments to find conditions allowing the transformation shown in Scheme 2 to occur were carried out by using a combination of *trans*-**9** and acetic acid as an electrophile with bases in several solvents (Table 1). The best result was obtained with 2 equiv of $NaN(SiMe_3)_2$ (NaHMDS) in THF, which afforded enol silyl ether **13** with *Z*-geometry ($J_{4,5}$ = 5.6 Hz) in 73% yield. No products protonated at the stage of **4** and **5** were detected. Use of LDA or $KN(SiMe_3)_2$ (KHMDS) resulted in significant decomposition. Also, use of smaller amounts of a base resulted in recovery of considerable amounts of the starting material. The *E*-isomer could not be detected even with the addition of HMPA, suggesting that an internal chelation structure **14** is not responsible for the formation of the (*Z*)-isomer.[11] The stereochemistry of the process will be discussed later.

With this result in hand, we next examined the behavior of *trans*-**9** toward alkylation reaction. When *trans*-**9** was treated with NaHMDS (2 equiv) at −30 to 5 °C followed by the addition of MeI (1.1 equiv) at −15 °C, monomethylated product (*Z*)-**15a** was obtained in 63% yield (Scheme 4). Although the reaction with EtI gave a similar result, in the case of *i*-PrI, (*Z*)-**13**, a product of protonation, was obtained. To obtain information about the alkylation process (**6** → **7**), an alkylation reaction of (*Z*)-**13** was carried out with NaHMDS (Scheme 5). Reac-

(3) For reviews on Brook rearrangement, see: (a) Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*; John 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. For the use of Brook rearrangement in tandem bond formation strategies, see: (d) Moser, W. H. *Tetrahedron* **2001**, *57*, 2065−2084. Also, see: (e) Ricci, A.; Degl'Innocenti, A. *Synthesis* **1989**, 647−660. (f) Bulman Page, P. C.; Klair, S. S.; Rosenthal, S. *Chem. Soc. Rev.* **1990**, *19*, 147−195. (g) Qi, H.; Curran, D. P. In *Comprehensive Organic Functional Group Transformations*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Moody, C. J., Eds.; Pergamon: Oxford, UK, 1995; pp 409−431. (h) Cirillo, P. F.; Panek, J. S. *Org. Prep. Proc. Int.* **1992**, *24*, 553−582. (i) Patrocinio, A. F.; Moran, P. J. S. *J. Braz. Chem. Soc.* **2001**, *12*, 7−31.

(4) (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. (c) Matsumoto, M.; Masu, H.; Yamaguchi, K.; Takeda, K. *Org. Lett.* **2004**, *6*, 4367−4369.

(5) Recently cyclopropane ring opening by a carbanion generated by Brook rearrangement was reported. Clayden, J.; Watson, D. W.; Chambers, M. *Tetrahedron* **2005**, *61*, 3195−3203.

(6) Corbe1, B.; Durst, T. *J. Org. Chem.* **1976**, *41*, 3648−3650.

(7) (a) Huges, S.; Griffiths, G.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1253−1264. (b) Stirling, C. J. M. *Chem. Rev.* **1978**, *78*, 517−567.

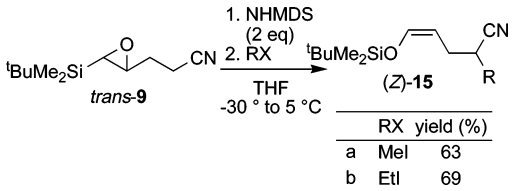
(8) For comparison of the α-anion stabilizing ability between phenyl group and trimethylsilyl group, see: Takeda, K.; Ubayama, H.; Sano, A.; Yoshii, E.; Koizumi, T. *Tetrahedron Lett.* **1998**, *39*, 5243−5246.

(9) Okugawa, S.; Takeda, K. *Org. Lett.* **2004**, *6*, 2973−2975.

(10) (a) Urabe, H.; Matsuka, T.; Sato, F. *Tetrahedron Lett.* **1992**, *33*, 4179−4182. (b) Chen, A. P.-C.; Chen, Y.-H.; Liu, H.-P.; Li, Y.-C.; Chen, C.-T.; Liang, P.-H. *J. Am. Chem. Soc.* **2002**, *124*, 15217−15224.

(11) This is also supported by the fact that (*Z*)-**13** was formed exclusively irrespective of the countercations. The difference in yield among Li, Na, and K as countercations cannot be explained at present, but possibly it may be due to the difference in the reactivity and stability of the carbanion based on the ionic character of the carbon−metal bond.

SCHEME 4. Alkylation of *trans*-9



SCHEME 5. Alkylation of (*Z*)-13

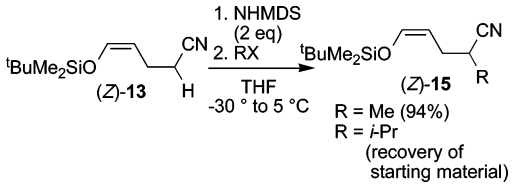
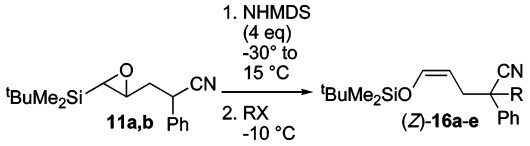


TABLE 2. Alkylation of 11



(*Z*)-**16a**−**e**	RX	yield (%)
a	MeI	84
b	EtI	73
c	*i*-PrI	65
d	CH_2=$CHCH_2Br$	75
e	$PhCH_2Br$	75

tion with MeI gave (*Z*)-**15a** in 94% yield, while reaction with *i*-PrI resulted in a recovery of (*Z*)-**13**, presumably due to competition with the elimination reaction.

When treated under the same conditions as those used for *trans*-**9**, **10** was recovered unchanged, suggesting that the malononitrile carbanion is too stable to attack at the epoxide carbon atom.

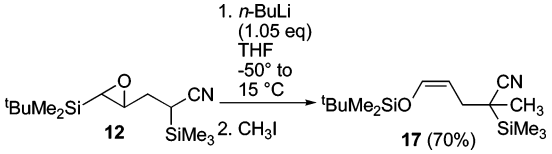
Next, we carried out the same reaction using **11** in which α-nitrile carbanion can be stabilized by the phenyl group. Treatment of a diastereomeric mixture of α-phenyl derivatives **11a**,**b** under reaction conditions similar to those used for **9** resulted in a recovery of the starting material, but use of 4 equiv of NaHMDS and elevated temperature (15 °C) gave (*Z*)-**16a**−**e** in good to excellent yields (Table 2). The reduced reactivity observed with **11** can be attributed to the phenyl-stabilized carbanion **4** (R = Ph), which is supported by the fact that treatment of **11a** and **11b**[12] separately with NaHMDS at −30 °C followed by quenching with AcOH afforded a mixture of **11a** and **11b** in the same ratio. This result also suggests that the ring-opening of the epoxide is the slowest step.

In contrast to the cases of *trans*-**9** and **11**, in the case of trimethylsilyl derivative **12** (diastereomeric mixture), use of *n*-BuLi was required to achieve a complete reaction probably because of the lower acidity[8] of the α-nitrile proton compared to that of phenyl derivative **11** and of steric congestion around the proton as shown in Scheme 6. The use of LDA or NaHMDS resulted in removal of the trimethylsilyl group.

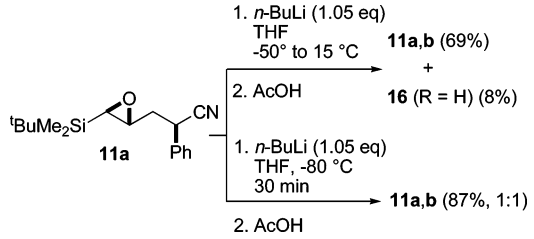
When **11a** was treated under the same conditions as those employed for **12**, a mixture of **11a** and **11b** was

(12) The relative stereochemistry was not determined.

SCHEME 6. Methylation of 12



SCHEME 7. Reaction of 11a with *n*-BuLi



obtained in 69% yield together with (*Z*)-**16** (R = H) (8%). On the other hand, treatment of **11a** with *n*-BuLi at −80 °C afforded a 1:1 mixture of **11a** and **11b** in 87% yield, indicating that an α-nitrile carbanion derived from α-phenyl derivative **11** is more stable than that obtained from α-trimethylsilyl derivative **12**, which is consistent with our previous results.[8]

The observed *Z*-selectivity in all cases can be explained by assuming the formation of silicate intermediate **18**[13,14] via backside displacement of the epoxide by the α-nitrile carbanion and the O−Si bond formation followed by concerted processes involving Brook rearrangement and the anti-mode of eliminative ring fission of the cyclopropane from the rotamer **19** (Scheme 8),[15] in which the C4−Si bond can adopt a coplanar arrangement with the C2−C3 bond. In this case, Brook rearrangement should occur with retention of configuration at the silyl-bearing carbon atom, because the (*E*)-derivative should be obtained if the rearrangement proceeds with inversion of configuration.[16] If our analysis for the stereoselectivity is correct, the use of *cis*-epoxide *cis*-**9** should provide (*E*)-enol silyl ether via **20**. To confirm this, we decided to examine the reaction of *cis*-**9**, which was prepared from *cis*-allyl alcohol **21**[4b] via the sequence shown in Scheme 9.

In fact, exposure of *cis*-**9** to NaHMDS followed by quenching with AcOH gave (*E*)-**13** in 62% yield (Table 3, entry 1). Alkylation also proceeded in the same way to afford (*E*)-**15a**,**b**. No (*Z*)-enol silyl ether derivative was detected. The observed stereospecificity is compatible with the concerted pathway indicated in Scheme 8.

Finally, to obtain further information about the stereochemistry of the ring-opening of cyclopropane, we

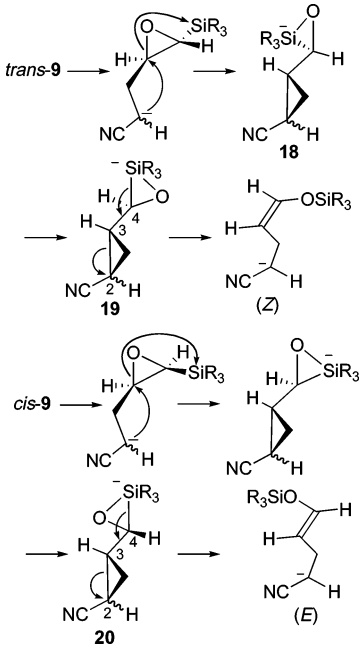
(13) Although the possibility of a silicate transition state cannot be excluded, we believe that the species is likely to be involved on the basis of our previous work and calculations[14] of the structure in the gas phase. Tanaka, K.; Masu, H.; Yamaguchi, K.; Takeda, K. *Tetrahedron Lett.* **2005**, *46*, 6429−6432.

(14) (a) Antoniotti, P.; Tonachini, G. *J. Org. Chem.* **1993**, *58*, 3622−3632. (b) Antoniotti, P.; Canepa, C.; Tonachini, G. *J. Org. Chem.* **1994**, *59*, 3952−3959. Also, see: (c) Fleming, I.; Lawrence, A. J.; Richardson, R. D.; Surry, D. S.; West, M. C. *Helv. Chim. Acta* **2002**, *85*, 3349−3365.

(15) Elimination reactions of α-oxidosilanes with a β-leaving group are known to proceed in an anti manner. Hudrlik, P. F.; Hudrlik, A. M.; Kulkarni, A. K. *J. Am. Chem. Soc.* **1985**, *107*, 4260−4264.

(16) For discussions on the stereochemistry of Brook rearrangement of α-silyl alkoxides bearing an α,β-leaving group, see: (a) Reich, H. J.; Holtan, R. C.; Bolm, C. *J. Am. Chem. Soc.* **1990**, *112*, 5609−5617. (b) Also, see ref. 5.

SCHEME 8. Stereochemical Processes of Base-Mediated Isomerization of *trans*- and *cis*-9



SCHEME 9. Preparation of *cis*-9

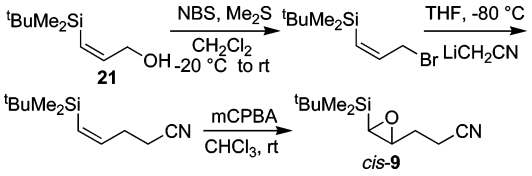
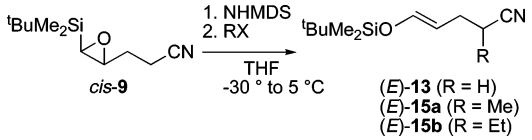


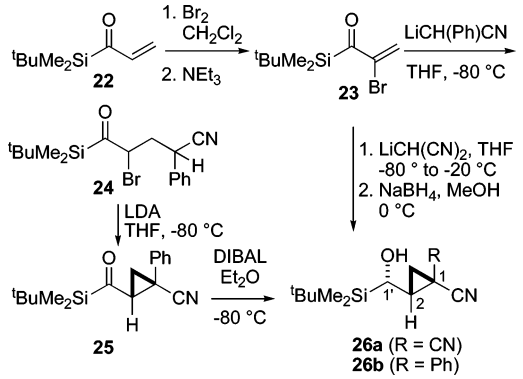
TABLE 3. Alkylation of *cis*-9



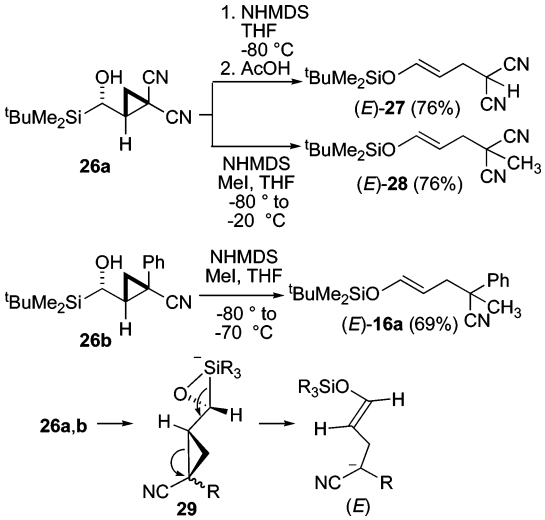
entry	RX	yield (%)
1	(AcOH)	62
2	MeI	71
3	EtI	54

decided to prepare α-silyl alcohol derivative **26**, a precursor for **5**, and to examine its Brook rearrangement-induced alkylation reaction. Although the parent substrate (R = H in **26a**) could not be prepared, dinitrile derivative **26a** and phenyl derivative **26b** were prepared from acryloylsilane **22**[17] by the route outlined in Scheme 10. While in the case of the dinitrile derivative the cyclopropane ring was formed directly from the reaction of α-bromoacryloysilane **23** with malononitrile anion, in the case of the phenyl derivative the reaction with benzyl cyanide anion resulted in the formation of addition product **24**, which was transformed into **26b**[18] by exposure to LDA followed by DIBAL reduction. Their stereochemistries were assigned on the basis of results of X-ray analysis of **26a**.

SCHEME 10. Preparation of 26a,b



SCHEME 11. Reaction of 26a and 26b



Although Brook rearrangement followed by ring opening in **26a** occurred instantly at −80 °C by treatment with NaHMDS to give (*E*)-**27**, methylation of the anion required a higher reaction temperature of −20 °C. On the other hand, methylation of phenyl derivative **26b** was completed at −80 to −70 °C to give (*E*)-**16a** (Scheme 11). The results suggest that the ring-opening of the cyclopropane is a much faster process than the other steps. The process, however, requires the presence of an anion-stabilizing group such as a nitrile group to proceed because the reaction of trimethylsilyl derivative **30**, prepared from β-trimethylsilylacryloysilane[19] by $NaBH_4$ reduction followed by Simmons−Smith reaction,[20] with NaHMDS did not afford the corresponding ring-opening product to give *O*-methylation derivative **31** (Scheme 12). Since the alkylation was completed at temperatures less than −20 °C even in the case of **26a**, the slowest step in the reaction cascade of **11** and **12** would be the anion-induced ring-opening of the epoxide. In the case of **9**, although the possibility of the slowest step of the ring opening of cyclopropane cannot be excluded, the slowest

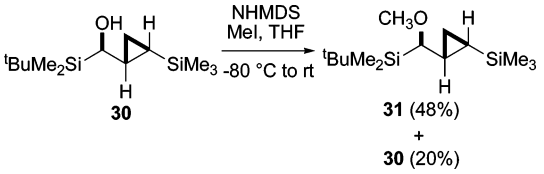
(17) Reich, H. J.; Kelly, M. J.; Olson, R. E.; Holtan, R. C. *Tetrahedron* **1983**, *39*, 949−960.

(18) **25** was obtained as a single isomer and the relative configurations of the nitrile-bearing carbon atom were assigned on the basis of NOESY correlations between the dimethyl group of TBS and the aromatic protons. The relative stereochemistry at C2 and C1′ in **26b** was assigned on the basis of literature analogy (ref 20).

(19) Takeda, K.; Nakajima, A.; Takeda, M.; Yoshii, E.; Zhang, J.; Boeckman, R. K., Jr. *Org. Synth.* **1999**, *76*, 199−213.

(20) (a) Sakaguchi, K.; Mano, H.; Ohfune, Y. *Tetrahedron Lett.* **1998**, *39*, 4311−4312. (b) Sakaguchi, K.; Higashino, M.; Ohfune, Y. *Tetrahedron* **2003**, *59*, 6647−6658.

SCHEME 12. Reaction of 30



step can also be the ring opening of the epoxide step since attempts to trap the cycropropane derivatives corresponding to **26a** (R = H) were unsuccessful. Also, the exclusive formation of (*E*)-isomers is consistent with the intermediary **29**, an intermediate corresponding to **20** (Scheme 8), which provides further support for our analysis of the stereochemical outcome of the reaction.

In conclusion, we have demonstrated that the reaction of δ-silyl-γ,δ-epoxypentanenitrile derivatives with a base and alkylating agents affords δ-siloxy-γ,δ-unsaturated pentanenitrile derivatives via nitrile anion cyclization with epoxysilanes, Brook rearrangement-mediated eliminative ring fissions of cyclopropanes, and α-alkylation of nitrile in a tandem fashion. We have also shown the stereochemical course of the reaction by the synthesis of proposed intermediates by an independent route and examination of the reaction to the products.

Experimental Section

(*E*)-(3-Bromoprop-1-enyl)-*tert*-butyldimethylsilane. To a cooled (0 °C) solution of NBS (13.6 g, 76.5 mmol) in CH_2Cl_2 (200 mL) was added dropwise Me_2S (6.70 mL, 91.8 mmol). The solution was stirred at the same temperature for 20 min and recooled to −15 °C before addition of a solution of 3-(*tert*-butyldimethylsilanyl)prop-2-en-1-ol (**8**) (8.80 g, 51.0 mmol) in CH_2Cl_2 (50 mL). The mixture was warmed to room temperarture and stirred for 3 h. The reaction mixture was poured into hexanes−Et_2O (1:1, 100 mL) and ice water (100 mL). Phases were separated and the aqueous phase was extracted with Et_2O. Combined organic phases were washed with saturated brine (100 mL), dried, and concentrated. The residual oil was filtered through a short pad of silica gel to give the title compound (6.18 g, 54%). Colorless oil, R_f 0.80 (hexane:AcOEt = 3:1). IR (film) 1610, 833 cm^{-1}. ^1H NMR (400 MHz) δ 0.05 (6H, s, $SiMe_2$), 0.88 (9H, s, *t*-Bu), 3.95 (2H, d, *J* = 6.8 Hz, H-3), 5.94 (1H, d, *J* = 18.4 Hz, H-1), 6.17 (1H, dt, *J* = 18.4, 6.8 Hz, H-2). ^{13}C NMR (100 MHz) δ −6.1, 16.7, 26.5, 35.2, 133.1, 142.3. MS 177 (M^+ − *t*-Bu).

(2*R,3*R**)-3-(3-(*tert*-Butyldimethylsilyl)oxiran-2-yl)-propanenitrile (*trans*-9).** To a cooled (−80 °C) solution of MeCN (806 μL, 15.4 mmol) in THF (80 mL) was added dropwise *n*-BuLi (2.25 M hexane, 6.80 mL, 15.3 mmol) and the solution was stirred at the same temperature for 10 min. This mixture was added to a solution of (*E*)-(3-bromoprop-1-enyl)-*tert*-butyldimethylsilane (3.00 g, 12.8 mmol) in THF (48 mL) via cannula over a period of 30 min. The reaction mixture was stirred at the same temperature for 5 min and diluted with 10% aqueous NH_4Cl solution (50 mL). Phases were separated and the aqueous phase was extracted with Et_2O (3 × 20 mL). Combined organic phases were washed with saturated brine (50 mL), dried, and concentrated to give crude (*E*)-4-(*tert*-butyldimethylsilyl)but-3-enenitrile (3.00 g).

This compound was dissolved in $CHCl_3$ (26 mL) and mCPBA (70%, 4.40 g, 17.8 mmol) was added. The reaction mixture was stirred at room temperature for 12 h, and diluted with Et_2O (50 mL) and saturated aqueous K_2CO_3 solution (50 mL). Phases were separated and the aqueous phase was extracted with Et_2O (2 × 20 mL). Combined organic phases were washed with saturated brine (50 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 60 g, elution with hexane:AcOEt = 3:1) to give *trans*-**9** (2.16 g, 80%). Colorless oil, R_f 0.41 (hexane:AcOEt = 2:1). IR (film) 2361 cm^{-1}. ^1H NMR (400 MHz) δ −0.05 and −0.02 (each 3H, s, $SiMe_2$), 0.95 (9H, s, *t*-Bu), 1.76−1.88 and 1.98−2.08 (each 1H, m, H-3), 2.14 (1H, d, *J* = 3.2 Hz, H-3′), 2.49 (2H, t, *J* = 7.2 Hz, H-2), 2.83−2.89 (1H, m, H-2′). ^{13}C NMR (100 MHz) δ −8.3, 14.3, 16.8, 26.6, 30.1, 50.2, 50.6, 119.2. HRMS calcd for $C_7H_{12}NOSi$ 154.0688 (M^+ − *t*-Bu), found 154.0702.

(2*R,3*R**)-2-((3-(*tert*-Butyldimethylsilyl)oxiran-2-yl)-methyl)malononitrile (10).** To a cooled (−80 °C) solution of malononitrile (284 μL, 5.12 mmol) in THF (35 mL) was added *n*-BuLi (2.25 M *n*-hexane, 2.28 mL, 5.12 mmol) and the mixture was stirred at the same temperature for 10 min before addition of a solution of (*E*)-(3-bromoprop-1-enyl)-*tert*-butyldimethylsilane (1.00 g, 4.27 mmol) in THF (5 mL). After being warmed to room temperature, the reaction mixture was poured into 10% aqueous NH_4Cl solution (20 mL) and extracted with Et_2O (10 mL × 3). Combined organic phases were washed with saturated brine (20 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 30 g, elution with hexane:AcOEt = 5:1) to give 2-((*E*)-3-(*tert*-butyldimethylsilyl)allyl)malononitrile (265 mg, 28%) and bis(3-(*tert*-butyldimethylsilyl)allyl)malononitrile (481 mg, 30%).

The monoalkylated product was dissolved in $CHCl_3$ (2.4 mL) and mCPBA (70%, 228 mg, 1.32 mmol) was added. The reaction mixture was stirred at room temperature for 12 h and diluted with Et_2O (5 mL) and saturated aqueous K_2CO_3 solution (10 mL). Phases were separated and the aqueous phase was extracted with Et_2O (3 × 5 mL). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 10 g, elution with hexane:AcOEt = 4:1) to give **10** (194 mg, 64%). Colorless oil, R_f 0.28 (hexane:AcOEt = 3:1). IR (film) 2258 cm^{-1}. ^1H NMR (500 MHz) δ −0.02 and −0.08 (each 3H, s, $SiMe_2$), 0.95 (9H, s, *t*-Bu), 2.15 (1H, ddd, *J* = 14.0, 7.1, 5.5 Hz, H-2), 2.24 (1H, d, *J* = 3.5 Hz, H-3′), 2.41 (1H, ddd, *J* = 14.0, 8.5, 3.5 Hz, H-2), 2.98 (1H, ddd, *J* = 7.1, 3.5, 3.5 Hz, H-2′), 3.93 (1H, dd, *J* = 6.8, 4.4 Hz, H-1). ^{13}C NMR (125 MHz) δ −8.4, −8.2, 16.7, 20.2, 26.5, 35.6, 50.9, 51.2, 112.2, 112.4. HRMS calcd for $C_8H_{11}N_2OSi$ 179.0641 (M^+ − *t*-Bu), found 179.0620.

(2*R,3*R**)-3-(3-(*tert*-Butyldimethylsilyl)oxiran-2-yl)-2-phenylpropanenitrile (11).** To a cooled (−80 °C) solution of benzyl cyanide (1.76 mL, 15.4 mmol) in THF (30 mL) was added *n*-BuLi (2.25 M *n*-hexane, 6.80 mL, 15.4 mmol) and the mixture was stirred at the same temperature for 10 min. This mixture was added to a cooled (−80 °C) solution of (*E*)-(3-bromoprop-1-enyl)-*tert*-butyldimethylsilane (3.00 g, 12.8 mmol) in THF (55 mL) via cannula over a period of 30 min and stirred at the same temperature for 5 min. The solution was diluted with 10% NH_4Cl solution (50 mL) and extracted with Et_2O (3 × 20 mL). Combined organic phases were washed with saturated brine (50 mL), dried, and concentrated to give crude (*E*)-5-(*tert*-butyldimethylsilyl)-2-phenylpent-4-enenitrile.

This compound was dissolved in $CHCl_3$ (26 mL) and mCPBA (70%, 4.40 g, 17.8 mmol) was added. The reaction mixture was stirred at room temperature for 12 h and diluted with Et_2O (50 mL) and saturated aqueous K_2CO_3 solution (50 mL). Phases were separated and the aqueous phase was extracted with Et_2O (3 × 20 mL). Combined organic phases were washed with saturated brine (50 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 60 g, elution with hexane:AcOEt = 3:1) to give **11** (2.56 g, 70%) as a 1:1 mixture of diastereomers. This mixture was separated by MPLC (elution with hexane:AcOEt = 1:2) to give **11a** (more polar) and **11b** (less polar). **11a**: Colorless oil, R_f 0.32 (hexane:AcOEt = 5:1). IR (film) 2245, 1601 cm^{-1}. ^1H NMR (400 MHz) δ −0.10 and −0.07 (each 3H, s, $SiMe_2$), 0.94 (9H, s, *t*-Bu), 2.08−2.13 (1H, m, H-3), 2.17 (1H, d, *J* = 3.6 Hz, H-3′), 2.24−2.32 (1H, m, H-3), 2.71−2.76 (1H, m, H-2′), 3.96 (1H, dd, *J* = 7.2, 7.2 Hz, H-2), 7.25−7.42 (5H, m, Ph). ^{13}C NMR

(100 MHz) δ −8.4, −8.2, 16.7, 26.6, 34.6, 39. 9, 50.4, 52.3, 120.5, 127.5, 128.5, 129.4, 134.9 (Ar). HRMS calcd for $C_{13}H_{16}NOSi$ 230.1001 ($M^+ - t$-Bu), found 230.0997. **11b**: Colorless oil, R_f 0.32 (hexane:AcOH = 5:1). IR (film) 2245, 1601 cm^{-1}. ^1H NMR (400 MHz) −0.03 and −0.01 (each 3H, s, $SiMe_2$), 0.95 (9H, s, *t*-Bu), 1.90−2.00 (1H, m, H-3), 2.16 (1H, d, J = 3.6 Hz, H-3′), 2.21−2.30 (1H, m, H-3), 2.98−3.05 (1H, m, H-2′), 4.03 (1H, dd, J = 10.4, 4.4 Hz, H-2), 7.37 (5H, m, Ar). ^{13}C NMR (100 MHz) δ −8.3, −8.0, 16.8, 26.7, 35.3, 41.2, 51.1, 52.9, 120.3, 127.2, 128.5, 129.4, 135.5. HRMS calcd for $C_{13}H_{16}NOSi$ 230.1001 ($M^+ - t$-Bu), found 230.1004.

3-((2*R,3*R**)-3-(*tert*-Butyldimethylsilyl)oxiran-2-yl)-2-(trimethylsilyl)propanenitrile (12).** To a cooled (−80 °C) solution of lithium diisopropylamide (LDA) prepared from diisopropylamine (939 μL, 6.7 mmol) and *n*-BuLi (2.3 M hexane, 2.91 mL, 6.7 mmol) in THF (23 mL) was added dropwise a solution of trimethylsilylacetonitrile (759 mg, 6.7 mmol) in THF (9 mL) and the solution was stirred at the same temperature for 10 min. This mixture was added to a cooled (−80 °C) solution of (*E*)-(3-bromoprop-1-enyl)-*tert*-butyldimethylsilane (1.50 g, 6.38 mmol) in THF (32 mL) via cannula over a period of 30 min and the reaction mixture was warmed to −60 °C. The solution was diluted with 10% NH_4Cl solution (100 mL) and extracted with hexane (2 × 50 mL). Combined organic phases were washed with saturated brine (50 mL), dried, and concentrated to give crude (*E*)-5-(*tert*-butyldimethylsilyl)-2-trimethylsilylpent-4-enenitrile.

This compound was dissolved in $CHCl_3$ (13 mL) and mCPBA (77%, 2.00 g, 8.9 mmol) was added. The reaction mixture was stirred at room temperature for 12 h, and diluted with Et_2O (20 mL) and saturated aqueous K_2CO_3 solution (20 mL). Phases were separated and the aqueous phase was extracted with Et_2O (3 × 10 mL). Combined organic phases were washed with saturated brine (20 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 45 g, elution with hexane:AcOEt = 8:1) to give **12** (1.29 g, 71%) as a 3:4 mixture of diastereomers. This mixture was separated with MPLC (elution with hexane:AcOEt = 15:1) to give **12a** (more polar) and **12b** (less polar). **12a**: Colorless needles (EtOH−H_2O), mp 64−65 °C, R_f 0.43 (hexane:AcOEt = 5:1). IR (KBr pellet) 2217 cm^{-1}. ^1H NMR (500 MHz) δ 0.03 (6H, s, $SiMe_2$), 0.18 (9H, s, $SiMe_3$), 0.95 (9H, s, *t*-Bu), 1.56 (1H, ddd, J = 14.0, 7.1, 3.4 Hz, H-3), 1.85 (1H, ddd, J = 14.0, 12.4, 4.4 Hz, H-3), 2.01 (1H, dd, J = 12.4, 3.4 Hz, H-2), 2.18 (1H, d, J = 3.4 Hz, H-3′), 2.95 (1H, ddd, J = 7.1, 4.4, 3.4 Hz, H-2′). ^{13}C NMR (125 MHz) δ −8.37, −8.17, −3.31, 16.4. 16.7, 26.6, 32.1, 51.2, 54.7, 121.6. HRMS calcd for $C_{10}H_{20}NOSi_2$ 226.1083 ($M^+ - t$-Bu), found 226.1084. Anal. Calcd for $C_{10}H_{20}NOSi_2$: C 59.30, H 10.31, N 4.94. Found: C 59.36, H 10.05, N 4.90. **12b**: Colorless prisms (EtOH−H_2O), mp 55−56 °C, R_f 0.43 (hexane:AcOH = 5:1). IR (KBr) 2217 cm^{-1}. ^1H NMR (500 MHz) δ −0.05 and −0.00 (each 3H, s, $SiMe_2$), 0.20 (9H, s, $SiMe_3$), 0.96 (9H, s, *t*-Bu), 1.70 (1H, ddd, J = 14.2, 5.5, 3.9 Hz, H-3), 1.81 (1H, dd, J = 10.8, 3.9 Hz, H-2), 2.02 (1H, ddd, J = 14.2, 10.8, 4.8 Hz, H-3), 2.12 (1H, d, J = 3.4 Hz, H-3′), 2.98 (1H, ddd, J = 5.5, 4.8, 3.4 Hz, H-2′). ^{13}C NMR (125 MHz) δ −8.35, −8.21, −3.16, 15.2. 16.7, 26.6, 30.9, 49.3, 54.4, 121.7. HRMS calcd for $C_{10}H_{20}NOSi_2$ 226.1083 ($M^+ - t$-Bu), found 226.1084.

Reaction of *trans*-9 with NaHMDS Followed by Quenching with Acetic Acid. To a cooled (−30 °C) solution of **9** (500 mg, 2.4 mmol) in THF (19 mL) was added NaHMDS (0.94 M THF, 5.1 mL, 4.8 mmol) and the reaction mixture was warmed to 5 °C before addition of AcOH (1 M THF, 4.8 mL, 4.8 mmol). The solution was diluted with 10% NH_4Cl solution (30 mL) and extracted with Et_2O (2 × 15 mL). Combined organic phases were washed with saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 15 g, elution with hexane:AcOEt = 10:1) to give (*Z*)-**13** (367 mg, 73%). R_f 0.54 (hexane:AcOEt = 3:1). IR (film) 2246, 1658 cm^{-1}. ^1H NMR (400 MHz) δ 0.14 (6H, s, $SiMe_2$), 0.92 (9H, s, *t*-Bu), 2.35−2.45 (4H, m, H-2 and H-3), 4.51 (1H, dt, J = 5.6, 5.2 Hz, H-4), 6.29 (1H, d, J = 5.6 Hz, H-5). ^{13}C NMR (100 MHz) δ −5.2, 17.6, 20.2, 18.4, 25.7, 105.6, 120.0, 141.5. HRMS calcd for $C_7H_{12}NOSi$ 154.0688 ($M^+ - t$-Bu), found 154.0678.

General Procedure for Alkylation of *trans*-9: Reaction of *trans*-9 with NaHMDS and MeI. To a cooled (−30 °C) solution of **9** (100 mg, 0.470 mmol) in THF (3.9 mL) was added NaHMDS (1.0 M THF, 0.94 mL, 0.94 mmol) and the reaction mixture was warmed to 5 °C. Then the mixture was cooled to −10 °C, and MeI (32 μL, 1.1 mmol) was added with stirring at the same temperature for 15 min before addition of 10% aqueous NH_4Cl solution (10 mL). The phases were separated, and the aqueous phase was extracted with Et_2O (3 × 5 mL). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 5 g, elution with hexane:AcOEt = 10:1) to give (*Z*)-**15a** (67 mg, 63%). Colorless oil. R_f 0.54 (hexane:AcOEt = 3:1). IR (film) 2243, 1658 cm^{-1}. ^1H NMR (400 MHz) δ 0.14 (6H, s, $SiMe_2$), 0.92 (9H, s, *t*-Bu), 1.29 (3H, d, J = 7.2 Hz, 2-Me), 2.37 (2H, dd, J = 6.8, 6.0 Hz, H-3), 2.50−2.68 (1H, m, 1H, H-2), 4.5 (1H, dt, J = 6.0, 6.0 Hz, H-4), 6.35 (1H, d, J = 6.0 Hz, H-5). ^{13}C NMR (100 MHz) δ −5.2, 17.6, 18.4, 25.7, 25.8, 28.3, 104.4, 123.3, 141.8. HRMS calcd for $C_8H_{14}NOSi$ 168.0845 ($M^+ - t$-Bu), found 168.0814.

General Procedure for Alkylation of 11: Reaction of 11 with NaHMDS and MeI. To a cooled (−30 °C) solution of a mixture of **11a** and **11b** (100 mg, 0.350 mmol) in THF (2.1 mL) was added NaHMDS (1.0 M THF, 1.40 mL, 1.40 mmol) and the reaction mixture was warmed to 15 °C. Then the mixture was cooled to −10 °C, and MeI (85 μL, 1.40 mmol) was added with stirring at the same temperature for 15 min before addition of 10% aqueous NH_4Cl solution (10 mL). The phases were separated, and the aqueous phase was extracted with Et_2O (3 × 5 mL). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 5 g, elution with hexane:AcOEt = 18:1) to give (*Z*)-**16a** (89 mg, 84%). Colorless oil. R_f 0.55 (hexane:AcOH = 5:1). IR (film) 2236, 1658, 1602 cm^{-1}. ^1H NMR (400 MHz) δ 0.12 and 0.13 (each 3H, s, $SiMe_2$), 0.93 (9H, s, *t*-Bu), 1.71 (3H, s, Me), 2.66−2.80 (2H, m, H-3), 4.45 (1H, dt, J = 6.0, 6.0 Hz, H-4), 6.32 (1H, d, J = 6.0 Hz, H-5), 7.25−7.49 (5H, m, Ph). ^{13}C NMR (100 MHz) δ −5.2, −5.2, 18.3, 25.8, 26.7, 36.3, 42.5, 103.3, 123.9, 125.8, 127.8, 128.9, 140.7, 142.0. HRMS calcd for $C_{14}H_{18}NOSi$ 244.3885 ($M^+ - t$-Bu), found 244.3848.

Reaction of 12 with *n*-BuLi and MeI. To a cooled (−50 °C) solution of **12** (80 mg, 0.28 mmol) in THF (2.8 mL) was added *n*-BuLi (2.3 M hexane, 130 μL, 0.3 mmol), and the reaction mixture was warmed to 15 °C. Then the mixture was cooled to −10 °C, and MeI (35 μL, 0.56 mmol) was added with stirring at the same temperature for 15 min before addition of 10% aqueous NH_4Cl solution (5 mL). The phases were separated, and the aqueous phase was extracted with hexane (3 × 5 mL). Combined organic phases were washed with saturated brine (5 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 4 g, elution with hexane:AcOEt = 10:1) to give **17** (58 mg, 70%). Pale yellow oil, R_f 0.45 (hexane:AcOEt = 5:1). IR (film) 1656, 2215 cm^{-1}. ^1H NMR (500 MHz) δ 0.12 and 0.12 (each 3H, s, $SiMe_2$), 0.17 (9H, s, $SiMe_3$), 0.90 (9H, s, *t*-Bu), 1.23 (3H, s, 2-Me), 2.29 (1H, ddd, J = 14.2, 8.2, 1.1 Hz, H-3), 2.35 (1H, ddd, J = 14.2, 6.6, 1.4 Hz, H-3), 4.60 (1H, ddd, J = 8.2, 6.6, 5.7 Hz, H-4), 6.37 (1H, ddd, J = 5.7, 1.4, 1.1 Hz, H-5). ^{13}C NMR (125 MHz) δ −5.32, −5.28, −4.22, 18.2, 18.3, 22.5, 25.6, 28.1, 104.4, 125.2, 141.3. HRMS calcd for $C_{11}H_{22}NOSi_2$ 240.1240 ($M^+ - t$-Bu), found 240.1242.

(*Z*)-(3-Bromoprop-1-enyl)-*tert*-butyldimethylsilane. To a cooled (0 °C) solution of DIBAL-H (31.5 mL, 177 mmol) in Et_2O was added dropwise 3-(*tert*-butyldimethylsilyl)-2-propyne-1-ol (10.0 g, 58.7 mmol) in Et_2O (13 mL). After refluxing for 2 h, the reaction mixture was cooled to −30 °C and a 10:1 mixture of Et_2O/MeOH (100 mL), water (100 mL), and 1 N

hydrochloric acid (50 mL) were added. Phases were separated and the aqueous phase was extracted with Et_2O (3 × 100 mL). Combined organic phases were washed with saturated brine, dried, and concentrated to give crude (*E*)-3-(*tert*-butyldimethylsilyl)-2-propene-1-ol. The product was used in the following step without further purification.

To a cooled (0 °C) solution of NBS (16.1 g, 90.5 mmol) in CH_2Cl_2 (120 mL) was added dropwise Me_2S (8.4 mL, 108.5 mmol). The solution was stirred at the same temperature for 20 min and cooled to −15 °C before addition of a solution of the above compound in CH_2Cl_2 (30 mL). The mixture was warmed to room temperature and stirred for 2 h. The reaction mixture was poured into hexanes−Et_2O (1:1, 100 mL) and ice water (200 mL). Phases were separated and the aqueous phase was extracted with hexane (2 × 100 mL). Combined organic phases were washed with saturated brine (100 mL), dried, and concentrated. The residual oil was filtered through a short pad of silica gel to give the title compound (8.24 g, 65%). Colorless oil, R_f 0.75 (hexane:AcOEt = 3:1). IR (film) 1601 cm^{-1}. ^1H NMR (400 MHz) δ 0.15 (6H, s, $SiMe_2$), 0.90 (9H, s, $SiMe_3$), 3.99 (2H, d, *J* = 8.1 Hz, H-3), 5.71 (1H, d, *J* = 13.9 Hz, H-1), 6.57 (1H, dt, *J* = 13.9, 8.1 Hz, H-2). ^{13}C NMR (100 MHz) δ −4.15, 17.0, 26.5, 32.3, 132.4, 143.5. MS 177 (M^+ − *t*-Bu).

3-((2*R,3*S**)-3-(*tert*-Butyldimethylsilyl)oxiran-2-yl)propanenitrile (*cis*-9).** To a cooled (−80 °C) solution of MeCN (537 μL, 10.2 mmol) in THF (43 mL) was added dropwise *n*-BuLi (2.3 M hexane, 4.43 mL, 10.2 mmol) and the solution was stirred at the same temperature for 10 min. This mixture was added to a solution of (*Z*)-(3-bromoprop-1-enyl)-*tert*-butyldimethylsilane (2.00 g, 8.5 mmol) in THF (43 mL) via cannula over a period of 30 min. The reaction mixture was stirred at the same temperature for 5 min and diluted with 10% aqueous NH_4Cl solution (50 mL). Phases were separated and the aqueous phase was extracted with hexane (3 × 20 mL). Combined organic phases were washed with saturated brine (50 mL), dried, and concentrated to give crude (*Z*)-4-(*tert*-butyldimethylsilyl)but-3-enenitrile.

This compound was dissolved in $CHCl_3$ (17 mL) and mCPBA (70%, 2.9 g, 11.9 mmol) was added. The reaction mixture was stirred at room temperature for 12 h, and diluted with Et_2O (20 mL) and saturated aqueous K_2CO_3 solution (20 mL). Phases were separated and the aqueous phase was extracted with Et_2O (10 mL × 2). Combined organic phases were washed with saturated brine (20 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 60 g, elution with hexane:AcOEt = 3:1) to give *cis*-**9** (1.19 g, 66%). Colorless oil, R_f 0.32 (hexane:AcOEt = 3:1). IR (film) 2248 cm^{-1}. ^1H NMR (400 MHz) δ 0.03 and 0.07 (each 3H, s, $SiMe_2$), 0.96 (9H, s, *t*-Bu), 1.57−1.66 (1H, m, H-3), 2.03−2.11 (1H, m, H-3), 2.36 (1H, d, *J* = 5.1 Hz, H-3′), 2.48−2.56 (2H, m, H-2), 3.16−3.20 (1H, m, H-2′). ^{13}C NMR (100 MHz) δ −6.15, −5.88, 15.2, 16.9, 26.6, 28.1, 49.1, 55.4, 119.1. HRMS calcd for $C_7H_{12}NOSi$ 154.0688 (M^+ − *t*-Bu), found 154.0688.

Reaction of *cis*-9 with NaHMDS Followed by Quenching with Acetic Acid. To a cooled (−30 °C) solution of *cis*-**9** (100 mg, 0.470 mmol) in THF (4.2 mL) was added NaHMDS (0.94 M THF, 1.0 mL, 0.94 mmol) and the reaction mixture was warmed to 5 °C before addition of AcOH (1 M THF, 0.94 mL, 0.94 mmol). The solution was diluted with 10% NH_4Cl solution (5 mL) and extracted with Et_2O (2 × 5 mL). Combined organic phases were washed with saturated brine (5 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 5 g, elution with hexane:AcOEt = 10:1) to give (*E*)-**13** (R = H) (62 mg, 62%). Colorless oil, R_f 0.48 (hexana:AcOEt = 5:1). IR (film) 1664, 2247 cm^{-1}. ^1H NMR (400 MHz) δ 0.15 (6H, s, $SiMe_2$), 0.92 (9H, s, *t*-Bu), 2.25 (2H, dt, *J* = 7.3, 6.6 Hz, H-3), 2.35 (2H, t, *J* = 6.6 Hz, H-2), 4.98 (1H, dt, *J* = 11.7, 7.3 Hz, H-4), 6.38 (1H, d, *J* = 11.7 Hz, H-5). ^{13}C NMR (100 MHz) δ −5.15, 18.4, 19.0, 25.1, 25.8, 107.1, 119.4, 143.2. HRMS calcd for $C_{11}H_{22}NOSi$ 212.1471 (M^+ + 1), found 212.1479.

General Procedure for Alkylation of *cis*-9: Reaction of *cis*-9 with NaHMDS and MeI. To a cooled (−30 °C) solution of *cis*-**9** (100 mg, 0.470 mmol) in THF (3.9 mL) was added NaHMDS (0.94 M THF, 1.0 mL, 0.94 mmol) and the reaction mixture was warmed to 5 °C. Then the mixture was cooled to −10 °C, and MeI (32 μL, 0.52 mmol) was added with stirring at the same temperature for 15 min before addition of 10% aqueous NH_4Cl solution (10 mL). The phases were separated, and the aqueous phase was extracted with Et_2O (3 × 5 mL). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 5 g, elution with hexane:AcOEt = 10:1) to give (*E*)-**15a** (75 mg, 71%). Colorless oil, R_f 0.52 (hexane:AcOEt = 3:1). IR (film) 1664, 2240 cm^{-1}. ^1H NMR (500 MHz) δ 0.13 (6H, s, $SiMe_2$), 0.90 (9H, s, *t*-Bu), 1.27 (3H, d, *J* = 7.1 Hz, 2-Me), 2.11−2.21 (2H, m, H-3), 2.57 (1H, ddq, *J* = 7.1, 7.1, 7.1 Hz, H-2), 4.97 (1H, ddd, *J* = 11.7, 7.8, 7.8 Hz, H-4), 6.34 (1H, d, *J* = 11.7 Hz, H-5). ^{13}C NMR (125 MHz) δ −5.22 ($SiMe_2$), 17.3 (Me), 18.3 (CMe_3), 25.7 (CMe_3), 26.8 (C-2), 32.2 (C-3), 105.7 (C-4), 122.7 (CN), 143.7 (C-5). HRMS calcd for $C_8H_{14}NOSi$ 168.0845 (M^+ − *t*-Bu), found 168.0842.

2-Bromo-1-(*tert*-butyldimethylsilyl)prop-2-enone (23). To a cooled (0 °C) solution of 1-(*tert*-butyldimethylsilyl)prop-2-enone (3.00 g, 17.6 mmol) in CH_2Cl_2 (59 mL) was added dropwise bromine (1.00 mL, 19.4 mmol) and the solution was stirred at the same temperature for 10 min. The solution was concentrated to give crude 2,3-dibromo-1-(*tert*-butyldimethylsilyl)propanone. The product was used in the following step without further purification.

To a cooled (0 °C) solution of the above compound in CH_2Cl_2 (176 mL) was added Et_3N (12 mL, 86.1 mmol) and the solution was stirred for 10 min. The mixture was diluted with 1 N HCl solution (100 mL) and extracted with hexane (3 × 50 mL). Combined organic phases were successively washed with saturated Na_2CO_3 solution and saturated brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 50 g, elution with hexane:AcOEt = 10:1) to give **23** (4.2 g, 96%). Orange oil, R_f 0.37 (hexane:CH_2Cl_2 = 2:1). IR (film) 1624 cm^{-1}. ^1H NMR (500 MHz) δ 0.31 (6H, s, $SiMe_2$), 0.93 (9H, s, *t*-Bu), 6.75 and 6.82 (each 1H, d, *J* = 2.5 Hz, H-3). ^{13}C NMR (125 MHz) δ −4.61, 17.1, 26.6, 132.0, 140.4, 224.6. MS 191 (M^+ − *t*-Bu).

(*tert*-Butyldimethylsilyl)-(2,2-dicianocyclopropyl)methanol (26a). To a cooled (−80 °C) solution of malononitrile (872 mg, 13.2 mmol) in THF (50 mL) was added dropwise *n*-BuLi (2.3 M hexane, 5.7 mL, 13.2 mmol) and the solution was stirred at the same temperature for 5 min before addition of a solution of **23** (3.00 g, 12.0 mmol) in THF (10 mL). After being warmed to −20 °C, the mixture was diluted with 10% NH_4Cl solution (100 mL) and extracted with hexane (2 × 50 mL). Combined organic phases were washed with saturated brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 60 g, elution with hexane:AcOEt = 3:1) to give 2-(*tert*-butyldimethylsilanecarbonyl)cyclopropane-1,1-dicarbonitrile (2.13 g, 76%). Yellow oil, R_f 0.37 (hexane:AcOEt = 5:1). IR (film) 1642, 2251 cm^{-1}. ^1H NMR (500 MHz) δ 0.29 and 0.30 (each 3H, s, $SiMe_2$), 0.97 (9H, s, *t*-Bu), 1.92 (1H, dd, *J* = 8.5, 5.3 Hz, H-4), 2.19 (1H, dd, *J* = 7.8, 5.3 Hz, H-4), 3.37 (1H, dd, *J* = 8.5, 7.8 Hz, H-2). ^{13}C NMR (125 MHz) δ −7.45, −7.37, 7.02, 17.0, 21.3, 26.4, 36.8, 111.6, 114.5, 234.9. HRMS calcd for $C_8H_9N_2OSi$ 177.0484 (M^+ − *t*-Bu), found 177.0453.

To a cooled (0 °C) solution of the above compound (80 mg, 0.34 mmol) in MeOH/THF (1:10, 3.4 mL) was added $NaBH_4$ (3 mg, 0.085 mmol) and the solution was stirred at the same temperature for 15 min. The reaction mixture was diluted with 10% NH_4Cl solution (10 mL) and extracted with Et_2O (3 × 5 mL). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 3 g, elution with hexane:AcOEt = 4:1) to give **26a** (30 mg, 30%). Colorless needles (Et_2O−hexane), mp 107−109 °C, R_f 0.35 (hexane:

AcOEt = 5:1). IR (KBr) 2254, 3484 cm^{-1}. ^1H NMR (500 MHz) δ 0.045 and 0.14 (each 3H, s, $SiMe_2$), 0.98 (9H, s, *t*-Bu), 1.62 (1H, dd, J = 8.5, 6.2 Hz, H-4), 1.85 (1H, d, J = 5.1 Hz, OH), 2.0 (1H, dd, J = 9.2, 6.2 Hz, H-4), 2.32 (1H, ddd, J = 11.0, 9.2, 8.5 Hz, H-2), 3.21 (1H, dd, J = 11.0, 5.1 Hz, H-1). ^{13}C NMR (125 MHz) δ −8.37, −6.96, 4.23, 16.9, 23.5, 26.9, 36.9, 64.9, 114.4, 115.3. HRMS calcd for $C_8H_{11}N_2OSi$ 179.0641 (M^+ − *t*-Bu), found 179.0634. Anal. Calcd for $C_8H_{11}N_2OSi$: C 60.97, H 8.53, N 11.85. Found: C 60.92, H 8.49, N 11.74. X-ray data: crystal system, monoclinic; space group, $P2(1)/c$; unit cell dimensions, a = 18.120(7) Å, α = 90°, b = 6.607(2) Å, β = 107.072(5)°, c = 12.804(5) Å; volume, 1465.4(9) $Å^3$; Z = 4; R = 0.061.

2-(*tert*-Butyldimethylsilanecarbonyl)-1-phenylcyclopropanecarbonitrile (25). To a cooled (−80 °C) solution of benzyl cyanide (515 mg, 4.40 mmol) in THF (37 mL) was added dropwise *n*-BuLi (2.25 M hexane, 1.96 mL, 4.40 mmol) and the solution was stirred at the same temperature for 15 min before addition of a solution of **23** (1.0 g, 4.01 mmol) in THF (3 mL). After being warmed to −60 °C, the mixture was diluted with 10% NH_4Cl solution (30 mL) and extracted with Et_2O (3 × 20 mL). Combined organic phases were washed with saturated brine (30 mL), dried, and concentrated to give **24**. This was used in the following step without further purification.

To a cooled (−80 °C) solution of lithium diisopropylamide (LDA) prepared from diisopropylamine (560 μL, 4.01 mmol) and *n*-BuLi (2.25 M hexane, 1.78 mL, 4.01 mmol) in THF (25 mL) was added dropwise a solution of the above compound in THF (15 mL). After being warmed to −60 °C, the reaction mixture was diluted with 10% NH_4Cl solution (30 mL) and extracted with Et_2O (3 × 20 mL). Combined organic phases were washed with saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 30 g, elution with hexane:AcOEt = 10:1) and MPLC (elution with hexane:AcOEt = 10:1) to give **25** (36 mg, 3%). Yellow oil, R_f 0.52 (hexane:AcOEt = 3:1). IR (film) 1663, 2239 cm^{-1}. ^1H NMR (500 MHz) δ 0.24 and 0.27 (each 3H, s, $SiMe_2$), 0.96 (9H, s, *t*-Bu), 1.75 (1H, dd, J = 7.8, 5.0 Hz, H-4), 2.36 (1H, dd, J = 7.1, 5.0 Hz, H-4), 3.06 (1H, dd, J = 7.8, 7.1 Hz, H-2), 7.31−7.42 (5H, m, Ph). ^{13}C NMR (100 MHz) δ −7.38, −7.28, 17.0, 20.9, 24.7, 26.4, 41.5, 118.2, 126.0, 128.3, 129.2, 135.0, 237.9. HRMS calcd for $C_{17}H_{23}NOSi$ 285.1554 (M^+), found 285.1552.

(*tert*-Butyldimethylsilyl)-(2-cyano-2-phenylcyclopropyl)methanol (26b). To a cooled (−80 °C) solution of **25** (36 mg, 0.126 mmol) in THF was added dropwise DIBAL-H (0.95 M hexane, 146 μL, 0.139 mmol), and the solution was stirred at the same temperature for 30 min before addition of MeOH (0.3 mL) and water (0.3 mL). The mixture was diluted with 10% NH_4Cl solution (5 mL) and extracted with Et_2O (3 × 5 mL). Combined organic phases were washed with saturated brine (5 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 500 mg, elution with hexane:AcOEt = 5:1) to give **26b** (25 mg, 69%). Pale yellow oil, R_f 0.21 (hexane:AcOEt = 5:1). IR (film) 1602, 1635, 1722, 2236, 3483 cm^{-1}. ^1H NMR (500 MHz) δ 0.05 and 0.12 (each 3H, s, $SiMe_2$), 1.00 (9H, s, *t*-Bu), 1.53 (1H, dd, J = 7.3, 5.7 Hz, H-4), 1.71 (1H, dd, J = 8.7, 5.7 Hz. H-4), 1.85 (1H, ddd, J = 11.2, 8.7, 7.3 Hz, H-2), 1.97 (1H, br, 1-OH), 3.41 (1H, d, J = 11.2 Hz, H-1), 7.27−7.40 (5H, m, Ph). ^{13}C NMR (125 MHz) δ −8.3, −6.9, 16.9, 20.6, 22.8, 27.0, 35.9, 66.8, 121.5, 126.3, 127.8, 129.0, 136.0. HRMS calcd for $C_{13}H_{16}NOSi$ 230.1001 (M^+ − *t*-Bu), found 230.0967.

Reaction of 26a with NaHMDS Followed by Quenching with Acetic Acid. To a cooled (−80 °C) solution of **26a** (10 mg, 0.04 mmol) in THF (0.4 mL) was added NaHMDS (0.94 M THF, 48 μL, 0.044 mmol), and the solution was stirred at the same temperature for 5 min before addition of AcOH (1.0 M THF, 44 μL, 0.044 mmol). The reaction mixture was diluted with water (2 mL) and extracted with Et_2O (3 × 2 mL). Combined organic phases were washed with saturated brine (2 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 1 g, elution with hexane:AcOEt = 5:1) to give (*E*)-**27** (7.6 mg, 76%). Colorless oil, R_f 0.36 (hexane:AcOEt = 5:1). IR (film) 1664, 2254 cm^{-1}. ^1H NMR (500 MHz) δ 0.17 (6H, s, $SiMe_2$), 0.92 (9H, s, *t*-Bu), 2.62 (2H, ddd, J = 8.0, 6.4, 1.2 Hz, H-3), 3.65 (1H, t, J = 6.4 Hz, H-2), 5.00 (1H, dt, J = 11.9, 8.0 Hz, H-4), 6.52 (1H, dt, J = 11.9, 1.2 Hz, H-5). ^{13}C NMR (100 MHz) δ −5.34, 24.6, 25.5, 26.7, 30.1, 101.8, 112.9, 146.6. HRMS calcd for $C_8H_{11}N_2OSi$ 179.0639 (M^+ − *t*-Bu), found 179.0641.

Reaction of 26a with NaHMDS and MeI. To a cooled (−80 °C) solution of **26a** (50 mg, 0.21 mmol) and CH_3I (14 μL, 0.23 mmol) in THF (1.9 mL) was added NaHMDS (0.94 M THF, 0.24 mL, 0.23 mmol). After being warmed to −20 °C, the reaction mixture was diluted with 10% NH_4Cl solution (5 mL) and extracted with Et_2O (3 × 5 mL). Combined organic phases were washed with saturated brine (5 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 2 g, elution with hexane:AcOEt = 5:1) to give (*E*)-**28** (40 mg, 76%). Colorless oil, R_f 0.46 (hexane:AcOEt = 5:1). IR (film) 1663, 2251 cm^{-1}. ^1H NMR (500 MHz) δ 0.16 (6H, s, $SiMe_2$), 0.92 (9H, s, *t*-Bu), 1.73 (3H, s, 2-Me), 2.53 (2H, dd, J = 8.0, 0.9 Hz, H-3), 5.00 (1H, dt, J = 11.9, 8.0 Hz, H-4), 6.49 (1H, dt, J = 11.9, 0.9 Hz, H-5). ^{13}C NMR (125 MHz) δ −5.23, 18.4, 23.7, 25.6, 33.0, 38.0, 101.1, 116.2, 147.1. HRMS calcd for $C_9H_{13}N_2OSi$,193.0797 (M^+ − *t*-Bu), found 179.0818.

Reaction of 26b with NaHMDS and MeI. To a cooled (−80 °C) solution of **26b** (35 mg, 0.12 mmol) and CH_3I (15 μL, 0.24 mmol) in THF (1.1 mL) was added dropwise NaHMDS (0.94 M THF, 143 μL, 0.134 mmol). After being warmed to −70 °C, the reaction mixture was diluted with 10% NH_4Cl solution (5 mL) and extracted with Et_2O (3 × 5 mL). Combined organic phases were washed with saturated brine (5 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 2 g, elution with hexane:AcOEt = 10:1) to give (*E*)-**16a** (25 mg, 69%). Pale yellow oil, R_f 0.44 (hexane:AcOEt = 8:1). IR (film) 1660, 1730, 2243 cm^{-1}. ^1H NMR (500 MHz) δ 0.08 (6H, s, $SiMe_2$), 0.87 (9H, s, *t*-Bu), 1.69 (3H, s, 2-Me), 2.44 (1H, ddd, J = 14.2, 8.2, 0.9 Hz, H-3), 2.49 (1H, ddd, J = 14.2, 7.6, 1.1 Hz, H-3), 4.86 (1H, ddd, J = 11.9, 8.2, 7.6 Hz, H-4), 6.25 (1H, dt, J = 11.9, 1.1, 0.9 Hz, H-5). ^{13}C NMR (125 MHz) δ −5.32, 18.2, 25.6, 26.2, 40.8, 43.1, 104.3, 123.3, 125.7, 127.7, 128.8, 140.0, 144.4. HRMS calcd for $C_{14}H_{18}$-NOSi 244.1158 (M^+ − *t*-Bu), found 244.1133.

(*tert*-Butyldimethylsilyl)-(2-trimethylsilanylcyclopropyl)methanol (30). To a cooled (−15 °C) solution of 1-(*tert*-butyldimethylsilyl)-3-trimethylsilylpropenone (2.00 g, 8.2 mmol) in MeOH/THF (1:10, 82 mL) was added $NaBH_4$ (310 mg, 8.2 mmol) and the solution was stirred at the same temperature for 10 min. The reaction mixture was diluted with 10% NH_4-Cl solution (50 mL) and extracted with Et_2O (3 × 30 mL). Combined organic phases were washed with saturated brine (50 mL), dried, and concentrated to give crude 1-(*tert*-butyldimethylsilyl)-3-trimethylsilylprop-2-en-1-ol. This was used in the following step without further purification.

To a cooled (−10 °C) solution of the above compound and CH_2I_2 (3.9 mL, 48.4 mmol) in CH_2Cl_2 (65 mL) was added dropwise $ZnEt_2$ (1.0 M hexane, 48.4 mL, 48.4 mmol) and the solution was stirred at the same temperature for 2 h. The reaction mixture was diluted with 10% NH_4Cl solution (50 mL) and extracted with Et_2O (3 × 30 mL). Combined organic phases were washed with saturated brine (50 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 60 g, elution with hexane:Et_2O = 3:1) to give **30** (1.17 g, 55%). Pale yellow oil, R_f 0.27 (hexane:Et_2O = 3:1). IR (film) 3462 cm^{-1}. ^1H NMR (500 MHz) δ −0.43 to −0.02 (1H, m, H-3), −0.05 (9H, s, $SiMe_3$), −0.02 and 0.05 (each 3H, s, $SiMe_2$), 0.39−0.42 (2H, m, H-4), 0.95 (9H, s, *t*-Bu), 0.97−1.03 (1H, m, H-2), 2.60 (1H, d, J = 10.1 Hz, H-1). ^{13}C NMR

(100 MHz) δ −8.56, −6.53, −2.11, 3.55, 7.78, 16.8, 20.9, 27.0, 71.6. HRMS calcd for $C_9H_{21}OSi_2$ 201.1131 ($M^+ - t$-Bu), found 201.1128.

(*tert*-Butyldimethylsilyl)-(2-trimethylsilanylcyclopropyl)methyl Methyl Ether (31). To a cooled (−80 °C) solution of **30** (100 mg, 0.41 mmol) and CH_3I (28 μL, 0.43 mmol) in THF (4.1 mL) was added NaHMDS (1.0 M THF, 0.43 mL, 0.43 mmol). After being warmed to room temperature, the solution was diluted with 10% NH_4Cl solution (10 mL) and extracted with Et_2O (3 × 5 mL). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 6 g, elution with hexane:Et_2O = 10:1) to give **30** (20 mg, 20%) and **31** (54 mg, 48%). Colorless oil, R_f 0.74 (hexane:AcOEt = 5:1). IR (film) 2951 cm^{-1}. ^1H NMR (500 MHz) δ −0.67−0.62 (1H, m, H-3), −0.05 and 0.03 (each 3H, s, $SiMe_2$), −0.04 (9H, s, $SiMe_3$), 0.54−0.57 (2H, m, H-4), 0.76−0.81 (1H, m, H-2), 0.92 (9H, s, *t*-Bu), 2.25 (1H, d, J = 9.9 Hz, H-1), 3.42 (3H, s, Me). ^{13}C NMR (125 MHz) δ −8.05, −5.58, −1.95, −0.47, 10.8, 16.7, 17.1, 27.1, 59.4, 81.2. HRMS calcd for $C_{10}H_{23}OSi_2$ 215.1287 ($M^+ - t$-Bu), found 215.1291.

Acknowledgment. This research was partially supported by a Grant-in-Aid for Scientific Research (B) 15390006, and a Grant-in-Aid for Scientific Research on Priority Areas 17035054 from the Ministry of Education, Culture, Sports, Science and Technology (MEXT). We thank the Research Center for Molecular Medicine, Faculty of Medicine, Hiroshima University and N-BARD, Hiroshima University for the use of their facilities.

Supporting Information Available: Full experimental details and spectral data and X-ray structural data for compound **26a** (CIF file). This material is available free of charge via the Internet at http://pubs.acs.org.

JO0519413