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Formation of 2-Cyano-2-siloxyvinylallenes via Cyanide-Induced Brook Rearrangement in γ-Bromo-α,β,γ,δ-unsaturated Acylsilanes

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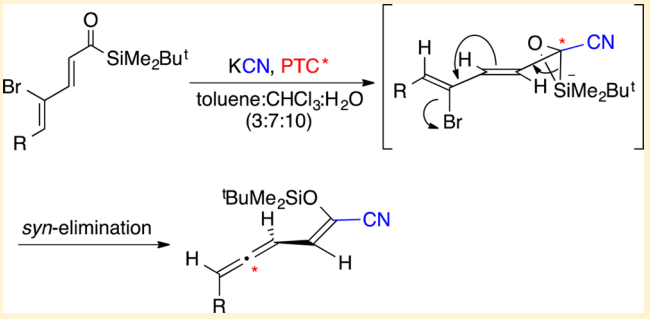
Supporting Information

ABSTRACT: Reactions of γ-bromo-α,β,γ,δ-unsaturated acylsilanes with KCN under phase-transfer catalyst conditions using *n*-Bu_4NBr afforded 2-cyano-2-siloxyvinylallenes via a tandem process that involves a nucleophilic attack of a cyanide ion and a Brook rearrangement induced conjugate vinylic 1,4-elimination. Use of a chiral cyanide ion source, derived from KCN and quaternary ammonium bromide derived from cinchona alkaloids, provided nonracemic allene derivatives. Based on this result and the reaction using a chiral hydride ion source, we propose a reaction pathway in which a Brook rearrangement mediated vinylic conjugate 1,4-elimination occurs in a *syn* alignment between the C−Br bond and C−Si bond in the silicate intermediate.

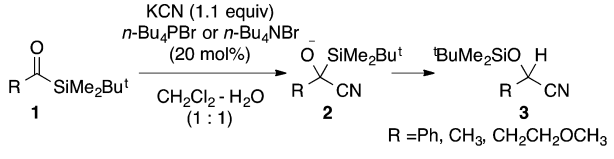


INTRODUCTION

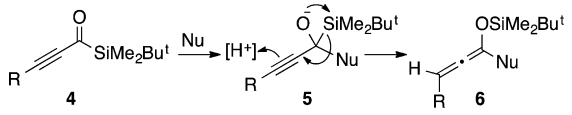
Reactions of acylsilanes with a cyanide ion can provide a unique means for generating α-metalated *O*-silylcyanohydrin via a Brook rearrangement facilitated by the anion-stabilizing capability of the cyano group.[1,2] The concept was first realized by Degl'Innocenti as a reaction of *n*-Bu_4NCN with acylsilanes, affording an anion of *O*-silyl cyanohydrin that can participate in 1,4-addition to α,β-unsaturated ketones.[3] The use of *n*-Bu_4NCN is based on the fact that conventional cyanide ion sources such as KCN are not sufficient because of their low solubility in common organic solvents to generate an appropriate concentration of the α-silyl alkoxide. We demonstrated that KCN can be effective for rearrangement under phase-transfer catalyst (PTC) conditions.[4] Thus, reaction with aroyl- or alkanoylsilanes **1** in a CH_2Cl_2−H_2O two-phase system at room temperature proceeds without quenching of the resulting α-silyl alkoxides **2** by water to give *O*-silyl cyanohydrin derivatives **3** (Scheme 1).

On the other hand, we have recently reported that a Meerwein−Ponndorf−Verley-type reduction[5] of alkynoylsilanes **4** via a hydride transfer from a chiral lithium amide (Scheme 2, Nu = H^-) affords siloxyallenes **6** via a Brook rearrangement in the resulting α-silyl alkoxide **5** followed by stereoselective protonation across the triple bond.[6] These findings led us to consider the possibility of employing a cyanide ion in place of a hydride as a nucleophile, which would afford allene derivatives bearing cyano and siloxy functions at the same carbon atom.[7]

Scheme 1. Reaction of Acylsilane with Potassium Cyanide under Phase-Transfer Catalytic Conditions



Scheme 2. Reaction of Alkynoylsilane with a Nucleophile



Regarding the use of a cyanide ion as a nucleophile in the reaction with acylsilanes, there is a concern about the reactivity of the carbanion generated by a Brook rearrangement. Thus, although the α-carbanion-stabilizing capability of a cyano group would facilitate the Brook rearrangement, it can also shift the equilibrium between the resulting allenyl and alkynylmethyl anions to the latter side and, as a result, can cause α-protonation of the cyano group but not of the lithioallene. In fact, attempted reactions of alkynoylsilanes **7** with KCN under catalytic conditions using KCN and a phase-transfer catalyst resulted in the formation of a complex mixture (Figure 1). To circumvent this problem, we considered the use of a substrate possessing a leaving group such as a halogen atom next to the resulting carbanion, which can force the formation a double bond by β-elimination. Reich reported that addition of organolithiums to α-halo-α,β-unsaturated acylsilanes generates

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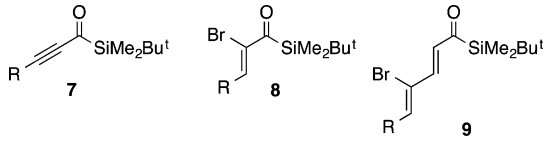


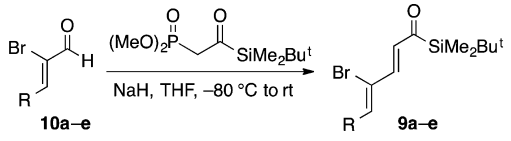
Figure 1. Acylsilane precursors for the generation of allenes.

α-silyl alkoxide, which can collapse to give allenol silyl ethers.[7d] We examined the reaction of α-bromoacryloyl derivative **8** with KCN under various conditions, but almost all of the reactions attempted resulted in recovery of the starting material or in the formation of a complex mixture. Since the failure of the reactions was partially attributed to a sterically congested environment in the transition state of β-elimination, we turned our attention to the use of a substrate **9** in which a double bond was introduced between the acylsilane moiety and the 1-bromovinyl group. Reactions of **9** with KCN would also provide 2-cyano-2-siloxyvinylallenes, which comprise a potentially useful building block, particularly for the synthesis of complex organic molecules via Diels–Alder and aldol reactions.[8]

RESULTS AND DISCUSSION

γ-Bromo-$\alpha,\beta,\gamma,\delta$-unsaturated acylsilanes **9a–e** were prepared by a Horner–Wadsworth–Emmons reaction[9] of the corresponding α-bromoacrolein derivatives, as shown in Scheme 3.

Scheme 3. Syntheses of γ-Bromo-$\alpha,\beta,\gamma,\delta$-unsaturated Acylsilanes 9a–e

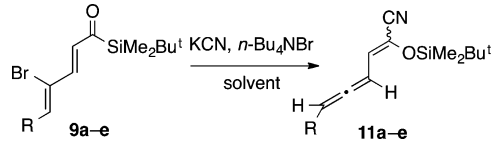


9a–e: R = Me (61%), Et (80%), *n*-Bu (82%), *t*-Bu (83%), Ph (83%)

Exploratory experiments were conducted using **9a** (R = Me). Application of previously optimized reaction conditions found for **1**, in which *n*-Bu_4PBr or *n*-Bu_4NBr as a PTC is used, provided **11a** in 73% and 71% yields, respectively (Table 1, entries 1 and 2). Since almost the same results were obtained with both of the PTCs, we chose *n*-Bu_4NBr for examination of reaction conditions by taking the ready availability of the corresponding chiral variants into consideration, which may be needed to examine the reaction pathway (vide infra). The best result in terms of yield was obtained by a combination of KCN (2 equiv) and a solvent system (toluene/$CHCl_3$/H_2O = 3:7:10) to give **11a** in 92% yield and in an 88:12 *Z*/*E* ratio (Table 1, entry 7). In all cases, only a trace amount of the *O*-silyl cyanohydrin derivative, a Brook rearrangement–protonation product, was detected. The *Z*/*E* geometries of the products were assigned on the basis of NOESY experiments of the corresponding *N*-Boc-amine derived via DIBAL reduction, $NaBH_4$ reduction of the resulting imines to amine, and protection with a Boc group.

The *Z*-selectivity observed can be understood on the basis of our previous findings[10] that when a Brook rearrangement-generated carbanion can be stabilized by a cyano group across two double bonds, a silicate or an α-silyl alkoxide intermediate does not have a sufficient lifetime to allow it to rotate freely about the C–C bond and the Brook rearrangement occurs in the nearest conformation where the C–Si bond has a parallel

Table 1. Reactions of 9a–e with Potassium Cyanide under Phase-Transfer Catalytic Conditions

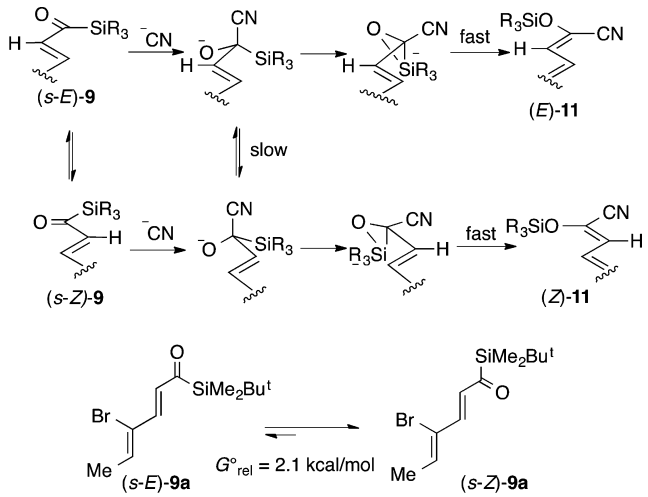


entry	9	R	KCN (equiv)	solvent	time (h)	yield (%)	*Z*/*E*
1[a]	**9a**	Me	1.1	CH_2Cl_2/H_2O (1:1)	3	73	90:10
2	**9a**	Me	1.1	CH_2Cl_2/H_2O (1:1)	3	71	88:12
3	**9a**	Me	1.1	$CHCl_3/H_2O$ (1:1)	7	86	85:15
4	**9a**	Me	1.1	Tol/H_2O (1:1)	24	79	83:17
5	**9a**	Me	1.1	Tol/$CHCl_3$/H_2O (7:3:10)	24	81	84:16
6	**9a**	Me	1.1	Tol/$CHCl_3$/H_2O (3:7:10)	11	93	85:15
7	**9a**	Me	2.0	Tol/$CHCl_3$/H_2O (3:7:10)	3	92	88:12
8	**9b**	Et	2.0	Tol/$CHCl_3$/H_2O (3:7:10)	2.5	82	85:15
9	**9c**	*n*-Bu	2.0	Tol/$CHCl_3$/H_2O (3:7:10)	3.5	86	86:14
10	**9d**	*t*-Bu	2.0	Tol/$CHCl_3$/H_2O (3:7:10)	4	93	86:14
11	**9e**	Ph	2.0	Tol/$CHCl_3$/H_2O (3:7:10)	2	47[b]	89:11

[a] *n*-Bu_4PBr was used. [b] The compound **11e** was unstable and decomposed during chromatographic purification.

alignment with the π orbital (Scheme 4). Thus, the dominant formation of *Z*–**11** indicates that the *s*-*Z* conformation in the

Scheme 4. Stereochemical Pathways for Reactions of 9 Leading to (*E*)- and (*Z*)-11



acylsilane moiety in **9** is more favorable than the *s*-*E* counterpart.[11] This was supported by DFT calculations (B3LYP/6-311++G(d,p) level) for **9a**, showing the former to be 2.1 kcal/mol more stable than the latter.[12,13] The formation of minor (*E*)-**11** can be explained by attack of a cyanide ion to a less favorable conformer (*s*-*E*)-**9** and/or by occurrence of a Brook rearrangement after a free rotation around the bond.

A possible mechanism for the formation of the allenes involves a Brook rearrangement induced vinylic 1,4-elimina-

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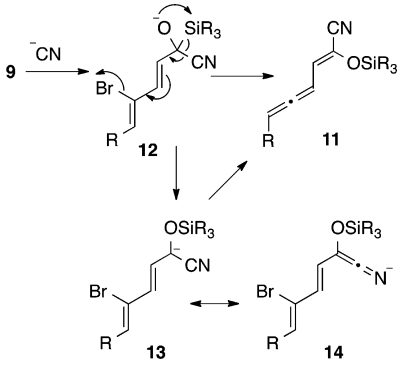
tion[14] that can occur either in a concerted (**12** → **11**) or a stepwise manner ($E1_{cb}$ like) via an α-nitrile carbanion **13** or a keteniminate **14** (Scheme 5). The fact that only a trace amount

Scheme 5. Possible Pathways of a Brook Rearrangement Followed by 1-4 Elimination



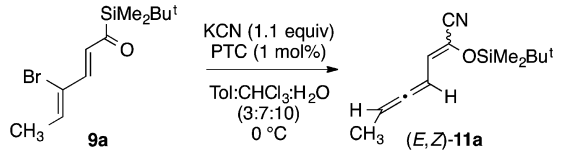
of *O*-silylcyanohydrin, a protonated product of **13**, was obtained in the reaction of **9** regardless of the presence of water suggests that the formation of allenes proceeds via a concerted pathway involving a Brook rearrangement followed by 1,4-elimination. In the concerted pathway, if the addition of a cyanide ion to (*s*-*Z*)-**9** takes place enantioselectively, chirality transfer from a central chirality at the stereogenic center to an axial chirality of the allene should occur to produce an enantioenriched allenylalkenyl silyl ether **11**. On the other hand, the stepwise mechanism via **13** or **14** should cause racemization.[15]

Since the stereochemical process of a Brook rearrangement induced vinylic 1,4-elimination such as **12** → **11** is unknown,[16] to gain some insight into these pathways, we decided to perform reactions using a chiral ammonium bromide in place of *n*-Bu_4NBr as a PTC and chose *N*-alkyl derivatives **15a**–**d** and **16** of cinchona alkaloids, which are readily available. Although ammonium salts derived from cinchona alkaloids have been extensively employed for an enantioselective alkylation,[17] desymmetrization,[18] Michael addition,[19] and others,[20] to the best of our knowledge, there is no precedent for the use as a chiral cyanide source in combination with KCN.[21,22]

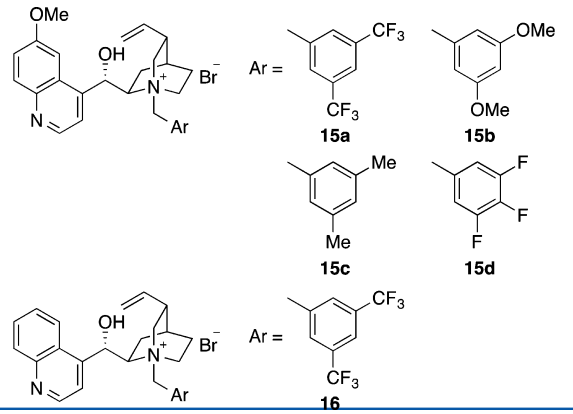
When **9a** was treated with KCN and **15a**–**d** and **16** under the conditions established for *n*-Bu_4NBr, the corresponding (*Z*)- and (*E*)-**11** were obtained in excellent yields and in nonracemic form (Table 2). The enantiomeric ratios (er's) were in the range 64:36–79:21. The absolute configuration of the major enantiomers was determined to be *R* on the basis of conversion of **11f** into known allenyl alcohol derivative **18** via an allenyl ester and comparison of the optical rotation with the literature value, $[\alpha]^{23}_D = -24.7$ (*c* 0.260, Et_2O) (lit.[23] $[\alpha]^{21}_D = -62.5$ (*c* 3.15, Et_2O), er = 87:13) (Scheme 6).

The moderate enantioselectivity observed suggests that there exists a pathway in which the addition of a cyanide ion to **9** takes place enantioselectively and a Brook rearrangement induced 1,4-elimination proceeds in a concerted manner (**12** → **11**) without the intermediacy of an α-nitrile carbanion **13** and a keteniminate **14**. Assuming that the chiral catalysts are unlikely to greatly affect the stereochemical outcome of the process involving a Brook rearrangement induced vinylic 1,4-elimination, the differences in the enantioselectivity observed should reflect the enantiofacial selectivity of a cyanide ion to an acylsilane carbonyl group. To determine whether the

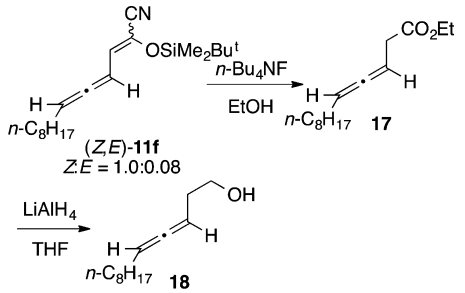
Table 2. Reactions of 9a–e with Potassium Cyanide under Chiral Phase-Transfer Catalytic Conditions



					er	
entry	PTC	time (h)	yield (%)	*Z*/*E*	(*Z*)-**11a**	(*E*)-**11a**
1	**15a**	1	90	81:19	79:21	76:24
2	**15b**	2	85	83:17	75:25	68:32
3	**15c**	0.75	84	88:12	72:28	68:32
4	**15d**	1.5	90	81:19	67:33	64:36
5	**16**	24	85	81:19	69:31	70:30



Scheme 6. Determination of Absolute Configuration of 11



enantiofacial selectivity in the attack of a cyanide ion controls the overall enantioselectivity, in situ trapping experiments of an α-cyano-α-silyl alkoxide by an electrophile including a cyanoformate and a chloroformate using **9a** were attempted but resulted in the formation of **11a** probably because of significant acceleration of the rearrangement due to the α-anion-stabilizing ability of a cyano group.

Although it was not possible to determine the direction and extent of the enantiofacial selectivity in the addition of a cyanide ion to acylsilane, the fact that (*R*,*Z*)-**11** are the major enantiomers in the 1,4-elimination of silicate intermediates **19** suggests two possible stereochemical pathways that involve *anti*-elimination from silicate intermediate (*R*)-**19** and *syn*-elimination from (*S*)-**19**, in which the terms "*syn*" and "*anti*" refer to the stereochemical relationship between the C–Br bond and the C–Si bond in a silicate intermediate **19** (Scheme 7).

To examine the mode of elimination (*syn*, *anti*),[24] the Brook rearrangement-mediated conjugate 1,4-elimination sequence was applied to enantioenriched α-silyl alcohol (*R*)-**21**, which

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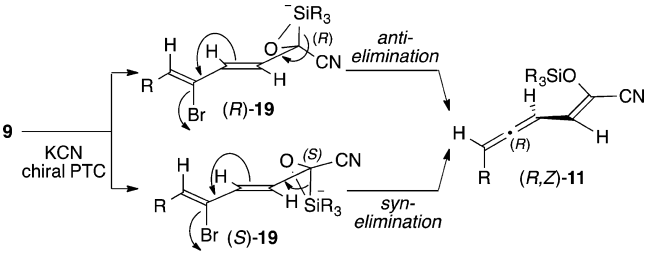
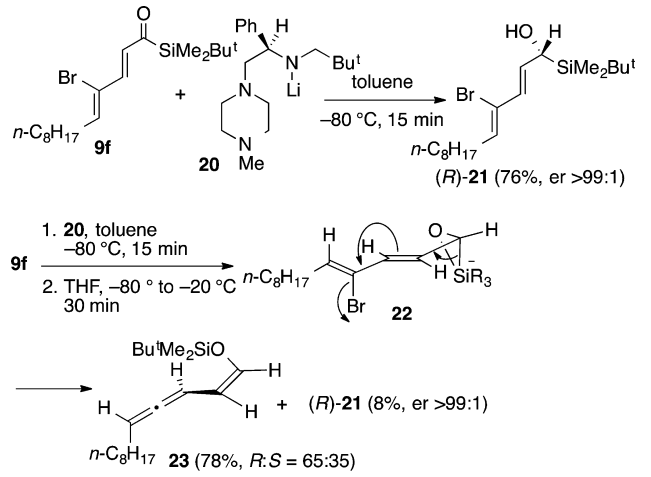
Scheme 7. Stereochemical Process of 1,4-Elimination in Silicate Intermediates 19



was obtained from acylsilane **9f** by Meerwein–Ponndorf–Verley-type reduction[5] by chiral lithium amide **20** (Scheme 8). Its absolute configuration was assigned by application of the modified Mosher method.[25]

Scheme 8. Stereochemical Process of the Reaction of 9f with Chiral Lithium Amide 20



Treatment of (*R*)-**21** with KOH/*n*-Bu_4NBr in toluene/$CHCl_3/H_2O$ (3:7:10) resulted in recovery of the starting material, probably because of deceleration by the change of a carbanion-stabilizing cyano group to hydrogen. Exposure of **9f**, however, to the usual reaction conditions, with the addition of THF after treatment with **20**, employed for the formation of siloxyallenes from alkynoylsilanes,[6] gave (*Z*)-**23** in 78% yield and in er 65:35 together with (*R*)-**21** (8%, er >99:1). The absolute configuration of the major enantiomer of (*Z*)-**23** was determined by chiral HPLC on comparison to an authentic sample.[26] The origin of the low er in comparison with those of **11** is not clear at present, but the stereochemical relationship between (*R*)-**21** and a major enantiomer (*R*)-**23** indicate that the major pathway involves a concerted conjugated *syn*-1,4-elimination in a silicate intermediate **22** as shown. Although these results cannot be directly applied to those for **19** because of the difference in the substituents (CN vs H), it is not unreasonable to suggest that the mode of the major pathway in the conjugate 1,4-elimination from **19** may also be *syn* and, accordingly, the absolute configuration of **19** is *S*.

CONCLUSION

We demonstrated that reactions of γ-bromo-α,β,γ,δ-unsaturated acylsilanes with KCN under PTC conditions provide 2-cyano-2-siloxyvinylallenes via a Brook rearrangement followed by a 1,4-conjugate elimination. Based on the results using a chiral cyanide source generated by a combination of KCN and chiral PTCs derived from cinchona alkaloids and the results of enantioselective reduction-induced conjugate 1,4-elimination, we have shown that the a concerted *syn*-mode elimination is possibly the major pathway in the cyanide-induced 1,4-conjugate elimination. It should be emphasized that a latent carbanion adjacent to a cyano group generated by a Brook rearrangement is able to participate in the vinylic 1,4-conjugate elimination. The finding that reactions using a chiral cyanide ion source provided nonracemic allene derivatives opens a new perspective in the enantioselective synthesis of highly functionalized allene derivatives.

EXPERIMENTAL SECTION

General Methods. All moisture-sensitive reactions were performed under a positive pressure of nitrogen. Anhydrous $MgSO_4$ was used for drying all organic solvent extracts in workup unless otherwise indicated, and removal of the solvents was performed with a rotary evaporator. Dry solvents and reagents were obtained by using standard procedures. Thin-layer chromatography was performed on precoated glass-backed silica gel 60 F-254 plates. For routine chromatography, the following adsorbents were used: silica gel 60N of particle size 63-210 μm or 40–50 μm. Liquid chromatography under medium pressures (MPLC) was carried out using prepacked columns (22 mm × 100 mm (5 μm silica gel) or 22 mm × 300 mm (10 μm silica gel)). ^1H NMR spectra (500 MHz) were taken in $CDCl_3$ with reference to $CHCl_3$ (δ 7.26) or in C_6D_6 with reference to C_6D_5H (δ 7.20) or in DMSO-d_6 with reference to $CD_2HS(O)CD_3$ (δ 2.49). ^{13}C NMR spectra (125 MHz) were measured in $CDCl_3$ with reference to the $CHCl_3$ (δ 77.2) or in C_6D_6 with reference to the C_6HD_5 (δ 128.0) or in DMSO-d_6 with reference to $CD_2HS(O)CD_3$ (δ 39.6 ppm). The assignment of ^1H and ^{13}C NMR spectra was based on H–H decoupling and HMQC experiments. HRMS spectra were obtained on a TOF mass spectrometer for **10d**, **10f**, and **11a** and on a LTQ-Orbitrap spectrometer for other compounds.

Preparation of α-Bromoacrolein Derivatives. (*Z*)-2-Bromobut-2-enal (**10a**),[27] (*Z*)-2-bromopent-2-enal (**10b**)[28], and (*Z*)-2-bromo-3-phenylacrylaldehyde (**10e**)[29] were prepared according to literature procedures.

*(Z)-2-Bromohept-2-enal (**10c**).*[30] To a cooled (0 °C) solution of (*E*)-hept-2-enal (2.0 mL, 14.4 mmol) in CH_2Cl_2 was slowly added a solution of Br_2 (775 μL, 15.1 mmol) in CH_2Cl_2 (7 mL). After the solution was stirred at the same temperature for 1 h, Et_3N (2.4 mL, 17.4 mmol) was slowly added. The solution was allowed to warm to room temperature over 30 min and stirred for 18 h. The reaction mixture was washed successively with 20% aqueous $Na_2S_2O_3$ (30 mL), 1 N HCl (30 mL), and saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 13 g, elution with hexane/Et_2O = 9:1) to give (*Z*)-2-bromohept-2-enal (1.0 g, 37%) as a pale yellow oil.

*(Z)-2-Bromo-4,4-dimethylpent-2-enal (**10d**).* To a solution of (*E*)-4,4-dimethylpent-2-en-1-ol (4.8 g, 42.4 mmol) in CH_2Cl_2 (84 mL) was added MnO_2 (18.4 g, 211.1 mmol). The mixture was refluxed for 24 h, filtered through a Celite pad, and concentrated to half of the original volume at 0 °C. The resulting mixture was diluted with CH_2Cl_2 (50 mL) and cooled to 0 °C. A solution of Br_2 (2.2 mL, 42.6 mmol) in CH_2Cl_2 (10 mL) was added slowly. After the solution was stirred at the same temperature for 1 h, Et_3N (7.1 mL, 51.1 mmol) was slowly added. The solution was allowed to warm to room temperature over 30 min and stirred for 18 h. The reaction mixture was washed successively with 20% aqueous $Na_2S_2O_3$ (50 mL), 1 N HCl (50 mL), and saturated brine (50 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 100 g, elution with hexane/Et_2O = 9:1) to give (*Z*)-2-bromo-4,4-dimethylpent-2-enal (5.83 g, 72%, two steps) as a pale yellow oil: R_f = 0.23 (hexane/Et_2O = 15:1); IR (NaCl) 3386, 2965, 2871, 2831, 2745, 2335, 1704, 1606 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (9H, s), 7.20 (1H, s), 9.09 (1H, s);

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^{13}C NMR ($CDCl_3$) δ 29.0, 35.1, 125.6, 164.5, 187.5; HRGC-TOFMS (FI) (m/z) calcd for $C_7H_{11}BrO$ 189.99933, found 190.00052.

*(Z)-2-Bromoundec-2-enal (**10f**).* The same procedure was followed as for **10c**. Compound **10f** was isolated in 88% yield (3.89 g, 15.74 mol): pale yellow oil; R_f = 0.23 (hexane/Et_2O = 15:1); IR (NaCl) 3384, 2926, 2857, 2735, 1702, 1617 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.86 (3H, t, J = 7.1 Hz), 1.25−1.38 (10 H, m), 1.54 (2H, tt, J = 7.3, 7.3 Hz), 2.51 (2H, td, J = 7.3, 7.1 Hz), 7.14 (1H, t, J = 7.1 Hz), 9.18 (1H, s); ^{13}C NMR ($CDCl_3$) δ 14.2, 22.7, 27.6, 29.2, 29.4, 29.4, 31.9, 32.2, 128.9, 156.1, 186.3; HRGC-TOFMS (FI) (m/z) calcd for $C_{11}H_{19}BrO$ 246.06193, found 246.06148.

Preparation of γ-Bromo-α,β,γ,δ-unsaturated Acylsilanes 9a−f. *Representative Procedure for the Preparation of (2E,4Z)-4-Bromo-1-(tert-butyldimethylsilyl)hexa-2,4-dien-1-one (**9a**).* To a cooled (0 °C) suspension of NaH (60%, 990 mg, 24.8 mmol) in THF (55 mL) was added a solution of dimethyl [2-(*tert*-butyldimethylsilyl)-2-oxoethyl]phosphonate[9] (6.3 g, 23.6 mmol) in THF (10 mL). The reaction mixture was allowed to warm to room temperature and stirred for 15 min. To the recooled (0 °C) mixture was added a solution of (*Z*)-2-bromobut-2-enal (3.84 g, 22.5 mmol) in THF (10 mL). The mixture was allowed to warm to room temperature over a period of 30 min, stirred for 2 h, and quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with Et_2O (10 mL × 3), and the combined organic phases were washed with saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 60 g, elution with hexane/CH_2Cl_2 = 2:1) to give **9a** (3.95 g, 61%). Recrystallization was performed to remove a trace amount of 4*E* isomer: orange needle; mp 47−48 °C (from hexane); R_f = 0.30 (hexane/CH_2Cl_2 = 2:1); IR (KBr) 3107, 3306, 2948, 2934, 2893, 2857, 1621, 1561 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.23 (6H, s), 0.93 (9H, s), 1.96 (3H, d, J = 6.9 Hz), 6.47 (1H, q, J = 6.9 Hz), 6.82 (1H, d, J = 14.9 Hz), 6.90 (1H, d, J = 14.9 Hz); ^{13}C NMR ($CDCl_3$) δ −6.5, 16.9, 18.4, 26.7, 125.7, 132.7, 137.8, 139.4, 235.4; HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{12}H_{21}BrOSi$ 289.0618, found 289.0621.

*(2E,4Z)-4-Bromo-1-(tert-butyldimethylsilyl)hepta-2,4-dien-1-one (**9b**):* orange oil; 80%, 614 mg (from 415 mg of **10b**); R_f = 0.39 (hexane/CH_2Cl_2 = 2:1); IR (NaCl) 2956, 2933, 2888, 2859, 2714, 1718, 1633, 1558 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.23 (6H, s), 0.93 (9H, s), 1.03 (3H, t, J = 7.6 Hz), 2.38 (2H, qd, J = 7.6, 7.1 Hz), 6.38 (1H, t, J = 7.1 Hz), 6.82 (1H, d, J = 14.9 Hz), 6.89 (1H, d, J = 14.9 Hz); ^{13}C NMR ($CDCl_3$) δ −6.5, 12.6, 16.9, 26.0, 26.7, 123.9, 132.9, 137.9, 146.0, 235.2; HRMS-APCI (m/z) [M + H]$^+$ calcd for $C_{13}H_{23}BrOSi$ 303.07743, found 303.07809.

*(2E,4Z)-4-Bromo-1-(tert-butyldimethylsilyl)nona-2,4-dien-1-one (**9c**):* orange oil; 82%, 968 mg (from 683 mg of **10c**); R_f = 0.19 (hexane/Et_2O = 29:1); IR (NaCl) 2955, 2931, 2860, 1633, 1558 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.23 (6H, s), 0.91 (3H, t, J = 7.3 Hz), 0.94 (9H, s), 1.36 (2H, qt, J = 7.3, 7.3 Hz), 1.46 (2H, tt, J = 7.6, 7.3 Hz), 2.38 (2H, td, J = 7.6, 7.3 Hz), 6.39 (1H, t, J = 7.3 Hz), 6.82 (1H, d, J = 14.7 Hz), 6.89 (1H, d, J = 14.7 Hz); ^{13}C NMR ($CDCl_3$) δ −6.5, 14.0, 16.9, 22.5, 26.7, 30.3, 32.4, 124.3, 132.8, 137.9, 145.0, 235.3; HRMS-APCI (m/z) [M + H]$^+$ calcd for $C_{15}H_{27}BrOSi$ 331.10873, found 331.10880.

*(2E,4Z)-4-Bromo-1-(tert-butyldimethylsilyl)-6,6-dimethylhepta-2,4-dien-1-one (**9d**):* orange plate; 83%, 978 mg (from 683 mg of **10d**); mp 62−64 °C (from hexane/Et_2O); R_f = 0.22 (hexane/Et_2O = 29:1); IR (KBr) 3255, 2956, 2930, 2898, 2858, 2745, 2714, 1631, 1552 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.22 (6H, s), 0.93 (9H, s), 1.25 (9H, s), 6.52 (1H, s), 6.84 (2H, s); ^{13}C NMR ($CDCl_3$) δ −6.6, 16.8, 26.6, 29.4, 34.6, 120.7, 132.2, 139.9, 153.5, 235.1; HRMS-APCI (m/z) [M + H]$^+$ calcd for $C_{15}H_{27}BrOSi$ 331.10873, found 331.10925.

*(2E,4Z)-4-Bromo-1-(tert-butyldimethylsilyl)-5-phenylpenta-2,4-dien-1-one (**9e**):* orange needle; 83%, 1.04 g (from 756 mg of **10e**); mp 90−93 °C (from hexane/CH_2Cl_2); R_f = 0.19 (hexane/CH_2Cl_2 = 2:1); IR (KBr) 3054, 2942, 2934, 2854, 1622, 1540 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.28 (6H, s), 0.97 (9H, s), 7.00 (1H, d, J = 14.6 Hz), 7.10 (1H, d, J = 14.6 Hz), 7.31 (1H, s), 7.35−7.42 (3H, m), 7.78 (2H, d, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ −6.5, 17.0, 26.8, 121.7, 128.5, 129.6, 130.2, 133.6, 135.1, 139.1, 140.3, 235.2; HRMS-APCI (m/z) [M + H]$^+$ calcd for $C_{17}H_{23}BrOSi$ 351.07743, found 351.07779.

*(2E,4Z)-4-Bromo-1-(tert-butyldimethylsilyl)trideca-2,4-dien-1-one (**9f**):* orange oil; 74%, 1.16 g (from 1.0 g of **10f**); R_f = 0.18 (hexane/Et_2O = 29:1); IR (NaCl) 2927, 2858, 1633, 1559 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.23 (6H, s), 0.87 (3H, t, J = 7.1 Hz), 0.94 (9H, s), 1.26−1.34 (10H, m), 1.46 (2H, tt, J = 7.6, 7.1 Hz), 2.37 (2H, dt, J = 7.6, 7.3 Hz), 6.40 (1H, t, J = 7.3 Hz), 6.82 (1H, d, J = 14.6 Hz), 6.90 (1H, d, J = 14.6 Hz); ^{13}C NMR ($CDCl_3$) δ −6.5, 14.3, 16.9, 22.8, 26.7, 28.2, 29.3, 29.5, 29.5, 32.0, 32.6, 124.3, 132.7, 137.8, 145.1, 235.3; HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{19}H_{35}BrOSi$ 387.17133, found 387.17160.

Representative Procedure for the Reaction of γ-Bromo-α,β,γ,δ-unsaturated Acylsilanes with KCN and n-Bu$_4$NBr (Table 1, Entry 7). To a cooled (0 °C) solution of KCN (45 mg, 0.69 mmol) and *n*-Bu_4NBr (11 mg, 34.6 μmol) in H_2O (3.5 mL) and CH_3Cl (2.5 mL) was added a solution of **9a** (100 mg, 0.346 mmol) in toluene (1.0 mL). After being stirred at the same temperature for 3 h, the mixture was diluted with H_2O (10 mL) and extracted with Et_2O (10 mL × 3). The combined organic phases were washed successively with H_2O (10 mL) and saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 5 g, elution with hexane/CH_2Cl_2 = 6:1) to give **11a** (71.7 mg, 92%, Z/E = 88:12).

*2-((tert-Butyldimethylsilyl)oxy)hepta-2,4,5-trienenitrile (**11a**):* colorless clear oil (Z/E = 88:12); R_f = 0.33 (hexane/Et_2O = 19:1); IR (NaCl) 3065, 2956, 2932, 2888, 2861, 2210, 1958, 1938, 1616 cm^{-1}; (*Z*)-**11a**: ^{1}H NMR (C_6D_6) δ 0.18 (3H, s), 0.19 (3H, s), 0.88 (9H, s), 1.42 (3H, dd, J = 7.1, 3.2 Hz), 5.09 (1H, qdd, J = 7.1, 7.1, 0.9 Hz), 5.67 (1H, dd, J = 11.0, 0.9 Hz), 6.20 (1H, ddq, J = 11.0, 7.1, 3.2 Hz); ^{13}C NMR (C_6D_6) δ −4.8, 13.5, 18.2, 25.4, 87.2, 87.8, 117.2, 122.3, 122.7, 209.9; (*E*)-**11a**: ^{1}H NMR (C_6D_6) δ 0.09 (6H, s), 0.87 (9H, s), 1.40 (3H, dd, J = 7.2, 3.1 Hz), 5.08 (1H, qdd, J = 7.2, 7.2, 1.0 Hz), 6.15 (1H, dd, J = 11.3, 1.0 Hz), 6.19 (1H, ddq, J = 11.3, 7.2, 3.1 Hz); ^{13}C NMR (C_6D_6) δ −5.0, −4.8, 13.7, 18.2, 25.4, 88.3, 88.6, 115.3, 124.1, 124.4, 209.9; HRMS-GC-FI (m/z) calcd for $C_{13}H_{21}ONSi$ 235.1392 found 235.1391.

*2-((tert-Butyldimethylsilyl)oxy)octa-2,4,5-trienenitrile (**11b**):* pale yellow oil (Z/E = 85:15); 82%, 64.3 mg (from 100 mg of **9b**); R_f = 0.35 (hexane/CH_2Cl_2 = 4:1); IR (NaCl) 3060, 2961, 2935, 2894, 2862, 2212, 1942, 1615 cm^{-1}; (*Z*)-**11b**: ^{1}H NMR (C_6D_6) δ 0.19 (3H, s), 0.19 (3H, s), 0.87 (3H, t, J = 7.3 Hz), 0.89 (9H, s), 1.82 (2H, qdd, J = 7.3, 7.3, 3.2 Hz), 5.23 (1H, tdd, J = 7.3, 6.4, 1.1 Hz), 5.71 (1H, dd, J = 11.0, 1.1 Hz), 6.27 (1H, ddt, J = 11.0, 6.4, 3.2 Hz); ^{13}C NMR (C_6D_6) δ −4.8, 13.2, 18.2, 21.7, 25.5, 88.4, 94.8, 117.3, 122.5, 122.6, 208.9; (*E*)-**11b**: ^{1}H NMR (C_6D_6) δ 0.10 (3H, s), 0.10 (3H, s), 0.86−0.87 (3H), 0.87 (9H, s), 1.79−1.85 (2H), 5.21−5.23 (1H), 6.08 (1H, dd, J = 11.2, 1.1 Hz), 6.24 (1H, ddt, J = 11.2, 6.2, 3.2 Hz); ^{13}C NMR (C_6D_6) δ −5.0, 13.2, 18.2, 21.8, 25.4, 89.8, 95.3, 115.3, 124.3, 124.3, 208.9; HRMS-APCI (m/z) [M + H]$^+$ calcd for $C_{14}H_{23}NOSi$ 250.16217, found 250.16205.

*2-((tert-Butyldimethylsilyl)oxy)deca-2,4,5-trienenitrile (**11c**):* colorless clear oil (Z/E = 86:14); 86%, 75.2 mg (from 110 mg of **9c**); R_f = 0.31 (hexane/CH_2Cl_2 = 6:1); IR (NaCl) 3061, 2955, 2934, 2862, 2212, 1942, 1616 cm^{-1}; (*Z*)-**11c**: ^{1}H NMR (C_6D_6) δ 0.19 (6H, s), 0.85 (3H, t, J = 7.1 Hz), 0.89 (9H, s), 1.19−1.30 (4H, m), 1.86 (2H, tdd, J = 6.9, 6.9, 3.0 Hz), 5.20 (1H, tdd, J = 6.9, 6.4, 0.9 Hz), 5.75 (1H, dd, J = 11.0, 0.9 Hz), 6.29 (1H, ddt, J = 11.0, 6.4, 3.2 Hz); ^{13}C NMR (C_6D_6) δ −4.8, 13.9, 18.2, 22.3, 28.2, 31.2, 87.8, 93.2, 117.3, 122.5, 122.6, 209.2; (*E*)-**11c**: ^{1}H NMR (C_6D_6) δ 0.10 (6H, s), 0.83−0.85 (3H), 0.87 (9H, s), 1.19−1.30 (4H, m), 1.84−1.89 (2H), 5.19−5.24 (1H), 6.10 (1H, dd, J = 11.4, 1.1 Hz), 6.23 (1H, ddt, J = 11.4, 6.2, 3.0 Hz); ^{13}C NMR (C_6D_6) δ −5.0, 13.9, 18.1, 22.3, 28.2, 31.2, 89.2, 93.6, 115.3, 124.3, 124.3, 209.2; HRMS-APCI (m/z) [M + H]$^+$ calcd for $C_{16}H_{27}NOSi$ 278.19347, found 278.19342.

*2-((tert-Butyldimethylsilyl)oxy)-7,7-dimethylocta-2,4,5-trienenitrile (**11d**):* pale yellow oil (Z/E = 86:14); 93%, 81.9 mg (from 110 mg of **9d**); R_f = 0.46 (hexane/CH_2Cl_2 = 3:1); IR (NaCl) 3060, 2959, 2898, 2864, 2212, 1941, 1615 cm^{-1}; (*Z*)-**11d**: ^{1}H NMR (C_6D_6) δ 0.19 (3H, s), 0.19 (3H, s), 0.89 (9H, s), 0.97 (9H, s), 5.26 (1H, d, J = 6.4 Hz), 5.74 (1H, d, J = 11.0 Hz), 6.33 (1H, dd, J = 11.0, 6.4 Hz); ^{13}C NMR (C_6D_6) δ −4.8, 18.2, 25.5, 30.0, 32.4, 89.5, 104.9, 117.3, 122.6, 124.4, 206.8; (*E*)-**11d**: ^{1}H NMR (C_6D_6) δ 0.10 (3H, s), 0.11 (3H, s),

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0.87 (9H, s), 0.97 (9H, s), 5.28 (1H, d, J = 6.1 Hz), 6.11 (1H, d, J = 11.4 Hz), 6.29 (1H, dd, J = 11.4, 6.1 Hz); ^{13}C NMR (C_6D_6) δ −5.0, −5.0, 18.1, 25.4, 30.0, 32.4, 90.9, 105.3, 115.3, 122.6, 124.3, 206.8; HRMS-APCI (m/z) $[M + H]^+$ calcd for $C_{16}H_{27}NOSi$ 278.19347, found 278.19348.

*(Z)-2-((tert-Butyldimethylsilyl)oxy)-6-phenylhexa-2,4,5-trienenitrile (**11e**):* pale yellow oil (Z/E = 89:11); 42%, 37.9 mg (from 100 mg of **9e**); R_f = 0.29 (hexane/CH_2Cl_2 = 4:1); IR (NaCl) 3060, 3029, 2951, 2936, 2894, 2860, 2211, 1931, 1603, 1584 cm^{-1}; (*Z*)-**11e**: ^{1}H NMR (C_6D_6) δ 0.19 (3H, s), 0.21 (3H, s), 0.89 (9H, s), 5.59 (1H, dd, J = 11.0, 1.0 Hz), 6.21 (1H, dd, J = 6.4, 1.0 Hz), 6.59 (1H, dd, J = 11.0, 6.4 Hz), 7.03−7.16 (5H, m); ^{13}C NMR (C_6D_6) δ −4.8, −4.8, 18.2, 25.4, 91.1, 97.0, 117.0, 120.5, 123.7, 127.5, 128.7, 129.0, 133.0, 211.7; (*E*)-**11e**: ^{1}H NMR (C_6D_6) δ 0.09 (3H, s), 0.10 (3H, s), 0.87 (9H, s), 6.02 (1H, dd, J = 11.5, 1.0 Hz), 6.21 (1H, dd, J = 6.4, 1.0 Hz), 6.54 (1H, dd, J = 11.5, 6.4 Hz), 7.03−7.16 (5H, m); ^{13}C NMR unable to assign ; HRMS-APCI (m/z) $[M + H]^+$ calcd for $C_{18}H_{23}NOSi$ 298.16217, found 298.16229.

Representative Procedure for the Reaction of γ-Bromo-α,β,γ,δ-unsaturated Acylsilanes with KCN and Chiral Phase-Transfer Catalyst (Table 2, Entry 1). To a cooled (0 °C) solution of KCN (24.8 mg, 0.38 mmol) and **15a** (2.2 mg, 3.4 μmol) in H_2O (3.4 mL) and CH_3Cl (2.4 mL) was added a solution of **9a** (100 mg, 0.34 mmol) in toluene (1.0 mL). After being stirred at the same temperature for 1 h, the mixture was diluted with H_2O (10 mL) and extracted with Et_2O (10 mL × 3). The combined organic phases were washed successively with H_2O (10 mL) and saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 5 g, elution with hexane/CH_2Cl_2 = 6:1) to give **11a** (67.1 mg, 90%, Z/E = 81:19). (*Z*)-**11a**: $[\alpha]^{22}_D$ −11.67 (*c* 1.00 $CHCl_3$). Chiralpak AS-3 (25 cm) + AS-H (15 cm), hexane, flow rate 0.4 mL/min, detection at 254 nm, t_R = 23.8 min (minor) and 31.1 min (major); (*E*)-**11a**: $[\alpha]^{23}_D$ −2.25 (*c* 0.185 $CHCl_3$). Chiralpak AS-3 (25 cm) + AS-H (15 cm), hexane, flow rate 0.4 mL/min, detection at 254 nm, t_R = 16.6 min (minor) and 19.1 min (major).

*2-((tert-Butyldimethylsilyl)oxy)tetradeca-2,4,5-trienenitrile (**11f**):* pale yellow oil (Z/E = 81:19); R_f = 0.24 (hexane/Et_2O = 49:1); $[\alpha]^{24}_D$ −12.86 (*c* 1.285, $CHCl_3$); IR (NaCl) 2928, 2858, 2212, 1942, 1615 cm^{-1}; (*Z*)-**11f**: ^{1}H NMR (C_6D_6) δ 0.19 (6H, s), 0.89 (9H, s), 0.95 (3H, t, J = 7.1 Hz), 1.25−1.34 (12H, m), 1.91 (2H, tdd, J = 6.9, 6.9, 3.0 Hz), 5.25 (1H, td, J = 6.9, 6.2 Hz), 5.76 (1H, d, J = 10.8 Hz), 6.29 (1H, ddt, J = 10.8, 6.2, 3.0 Hz); ^{13}C NMR (C_6D_6) δ −4.8, 14.3, 18.2, 23.0, 25.5, 28.5, 29.2, 29.4, 29.6, 29.7, 32.2, 87.9, 93.3, 117.3, 122.5, 122.6, 209.2; (*E*)-**11f**: ^{1}H NMR (C_6D_6) δ 0.11 (6H, s), 0.87 (9H, s), 0.95 (3H), 1.25−1.34 (12H), 1.91 (2H, tdd, J = 6.9, 6.9, 3.0 Hz), 5.25 (1H), 6.11 (1H, d, J = 11.3 Hz), 6.26 (1H, ddt, J = 11.3, 6.2, 3.0 Hz); ^{13}C NMR (C_6D_6) δ −5.0, 14.2, 18.1, 23.0, 25.4, 28.6, 29.2, 29.4, 29.6, 29.7, 32.2, 89.3, 93.7, 115.3, 124.3, 124.3, 209.3; HRMS-APCI (m/z) $[M + H]^+$ calcd for $C_{20}H_{35}ONSi$ 334.25607, found 334.25616.

Preparation of Chiral Phase-Transfer Catalysts. *Representative Procedure for the Preparation of **15b**.* To solution of quinidine (324 mg, 1.0 mmol) in toluene (10 mL) was added 1-(bromomethyl)-3,5-dimethoxybenzene (254 mg, 1.1 mmol). The mixture was stirred at 80 °C for 2 h, cooled to room temperature, and poured into Et_2O (80 mL). The precipitate that appeared was filtered and washed with Et_2O to afford **15b** (551 mg, 99%) as a white solid: mp 160 °C dec; R_f = 0.40 (CH_2Cl_2/MeOH = 9:1); $[\alpha]^{27}_D$ +202.33 (*c* 0.11, MeOH); IR (KBr) 3212, 2948, 2838, 1603, 1510; ^{1}H NMR (DMSO-d_6) δ 1.06−1.12 (1H, m), 1.70−1.78 (2H, m), 1.89 (1H, brs), 2.38 (1H, dd, J = 11.2, 11.2 Hz), 2.66 (1H, ddd, J = 8.7, 8.7, 8.7 Hz), 2.94 (1H, dd, J = 10.1, 10.0 Hz), 3.57 (1H, dd, J = 8.7, 8.7 Hz), 3.76 (1H, dd, J = 9.2, 9.2 Hz), 3.82 (6H, s), 3.98 (1H, dd, J = 10.1, 9.6 Hz), 4.06 (3H, s), 4.20 (1H, dd, J = 8.7, 8.7 Hz), 4.65 (1H, d, J = 12.4 Hz), 4.90 (1H, d, J = 12.4 Hz), 5.22 (1H, s), 5.25 (1H, d, J = 6.6 Hz), 6.02 (1H, ddd, J = 17.2, 8.7, 6.6 Hz), 6.49 (1H, brs), 6.70 (1H, s), 6.76 (1H, d, J = 3.7 Hz), 6.87(2H, d, J = 1.3 Hz), 7.40 (1H, d, J = 2.3 Hz), 7.49 (1H, dd, J = 9.2, 2.3 Hz), 7.75 (1H, d, J = 4.3 Hz), 8.00 (1H, d, J = 9.2 Hz), 8.80 (1H, d, J = 4.3 Hz); ^{13}C NMR (DMSO-d_6) δ 20.6, 23.2, 26.4, 36.8, 54.3, 55.6, 55.7, 56.2, 63.5, 64.7, 67.7, 101.6, 102.4, 111.8, 117.1, 120.4, 121.4, 125.5, 129.7, 131.5, 137.4, 143.6, 143.8, 147.5, 157.6, 160.7; HRMS-ESI (m/z) $[M]^+$ calcd for $C_{29}H_{35}N_2O_4$ 475.25913, found 475.25906.

*(1S,2R,4S,5R)-1-(3,5-Dimethylbenzyl)-2-((S)-hydroxy(6-methoxyquinolin-4-yl)methyl)-5-vinylquinuclidin-1-ium Bromide (**15c**):* 83%, 436 mg (from 324 mg of quinidine); white solid; mp 233 °C dec; R_f = 0.40 (CH_2Cl_2/MeOH = 9:1); $[\alpha]^{26}_D$ +223.67 (*c* 0.11, MeOH); IR (KBr) 3780, 3144, 3001, 2951, 1619, 1509; ^{1}H NMR (DMSO-d_6) δ 1.01−1.09 (1H, m), 1.70−1.81 (2H, m), 1.87 (1H, brs), 2.37 (6H, s), 2.38−2.41 (1H, m), 2.64 (1H, ddd, J = 8.7, 8.7, 8.7 Hz), 2.92 (1H, ddd, J = 10.6, 9.8, 9.8 Hz), 3.49 (1H, dd, J = 11.5, 8.7 Hz), 3.83 (1H, dd, J = 9.4, 9.4 Hz), 3.96 (1H, dd, J = 10.6, 10.6 Hz), 4.08 (3H, s), 4.18 (1H, dd, J = 11.5, 8.7 Hz), 4.67 (1H, d, J = 12.6 Hz), 4.97 (1H, d, J = 12.6 Hz), 5.21 (1H, s), 5.23 (1H, d, J = 4.3 Hz), 6.02 (1H, ddd, J = 17.4, 8.7, 4.3 Hz), 6.51 (1H, brs), 6.80 (1H, d, J = 3.9 Hz), 7.17 (1H, s), 7.30 (2H, s), 7.41 (1H, d, J = 2.5 Hz), 7.48 (1H, dd, J = 9.2, 2.5 Hz), 7.75 (1H, d, J = 4.4 Hz), 7.99 (1H, d, J = 9.2 Hz), 8.79 (1H, d, J = 4.4 Hz); ^{13}C NMR (DMSO-d_6) δ 20.7, 20.9, 23.2, 26.5, 36.8, 53.8, 55.8, 56.1, 63.3, 64.7, 67.3, 102.5, 117.1, 120.4, 121.4, 125.5, 127.6, 131.4, 131.4, 131.6, 137.4, 138.2, 143.6, 143.8, 147.5, 157.5; HRMS-ESI (m/z) $[M]^+$ calcd for $C_{29}H_{35}N_2O_2$ 443.26930 found 443.26920.

*(1S,2R,4S,5R)-2-((S)-Hydroxy(6-methoxyquinolin-4-yl)methyl)-1-(3,4,5-trifluorobenzyl)-5-vinylquinuclidin-1-ium Bromide (**15d**):* 85%, 453 mg (from 324 mg of quinidine); white solid; mp 233 °C dec; R_f = 0.40 (CH_2Cl_2/MeOH = 9:1); [a]$^{26}_D$ +190.65 (*c* 0.11, MeOH); IR (KBr) 3087, 3012, 2894, 2832, 1620, 1534, 1509; ^{1}H NMR (DMSO-d_6) δ 1.09−1.14 (1H, m), 1.75−1.81 (2H, m), 1.89 (1H, brs), 2.38 (1H, dd, J = 10.9, 10.9 Hz), 2.62 (1H, ddd, J = 8.0, 8.0, 8.0 Hz), 3.06 (1H, ddd, J = 10.1, 10.1, 10.1 Hz), 3.54 (1H, dd, J = 9.4, 8.0 Hz), 3.79 (1H, dd, J = 10.9, 10.9 Hz), 4.02−4.07 (1H, m), 4.07 (3H, s), 4.25 (1H, dd, 9.4, 8.0 Hz), 4.82 (1H, d, J = 12.6 Hz), 5.10 (1H, d, J = 12.6 Hz), 5.23 (1H, s), 5.26 (1H, d, J = 10.5 Hz), 6.01 (1H, ddd, 17.1, 10.5, 8.0 Hz), 6.47 (1H, brs), 6.77 (1H, d, J = 3.9 Hz), 7.42 (1H, d, J = 2.5 Hz), 7.48 (1H, dd, J = 9.2, 2.5 Hz), 7.75 (1H, d, J = 4.6 Hz), 7.89 (1H, d, J = 7.5 Hz), 7.90 (1H, d, J = 7.5 Hz), 8.00 (1H, d, J = 9.2 Hz), 8.79 (1H, d, J = 4.6 Hz); ^{13}C NMR (DMSO-d_6) δ 20.7, 23.1, 26.4, 37.0, 54.0, 55.9, 56.0, 61.4, 64.7, 67.8, 102.4, 117.1, 118.8, 119.0, 120.5, 121.4, 125.0, 125.6, 131.5, 137.3, 140.1 (J_{C-F} = 253.4 Hz), 143.4, 143.8, 147.4, 149.2, 151.2, 157.6; HRMS-ESI (m/z) $[M]^+$ calcd for $C_{27}H_{28}F_3N_2O_2$ 469.20974, found 469.20959.

Determination of *E*/*Z* Geometry of 11a. The assignment of *Z* stereochemistry is based on NOESY experiments of *tert*-butyl (*Z*)-(2-((*tert*-butyldimethylsilyl)oxy)hepta-2,4,5-trien-1-yl)carbamate (**24**).

To a cooled solution (−80 °C) of **11a** (200 mg, 0.850 mmol) in Et_2O (8.5 mL) was added DIBAL (1.02 M solution in hexane, 1.67 mL, 1,70 mmol). The mixture was allowed to warm to 0 °C over 1 h and then recooled to −80 °C. MeOH (4 mL) and then $NaBH_4$ (97 mg. 2.55 mmol) was added. The mixture was warmed to room temperature over 1 h and diluted with EtOAc (20 mL). The mixture was washed successively with 2 N HCl (15 mL) and saturated brine (15 mL), dried, and concentrated to give a crude compound (230.8 mg), which was used in the next step without purification.

To a cooled (0 °C) solution of the above product (230.8 mg) in CH_2Cl_2 (5.7 mL) were added Et_3N (237 μL, 1.70 mmol) and Boc_2O (200 μL, 0.935 mmol). The mixture was allowed to warm to room temperature and stirred for 4 h. Then 1-methylpiperazine (94 μL, 0.85 mmol) was added, and the mixture was stirred for 1 h. The mixture was then diluted with Et_2O (20 mL), washed successively with 1 N HCl (10 mL × 2), saturated $NaHCO_3$ (15 mL), and saturated brine (15 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 10 g, elution with hexane/Et_2O = 12:1) to give **24** (149.3 mg, 53%, 2 steps) as a colorless clear oil: R_f = 0.32 (hexane/Et_2O = 9:1); IR (NaCl) 3453, 3012, 2957, 2934, 2897, 2861, 1943, 1708, 1653, 1508; ^{1}H NMR (C_6D_6) δ 0.16 (6H, s), 0.97 (9H, s), 1.45 (9H, s), 1.58 (3H, dd, J = 7.1, 3.0 Hz), 3.67 (2H, d, J = 5.2 Hz), 4.24 (1H, brt), 5.25 (1H, qd, J = 7.1, 6.0 Hz), 5.34 (1H, d, J = 10.8 Hz), 6.42 (1H, ddq, J = 10.8, 6.0, 3.0 Hz); ^{13}C NMR (C_6D_6) δ −4.0, −3.9, 14.6, 18.4, 25.9, 28.4, 45.3, 78.9, 86.9, 88.4, 105.5, 148.5, 155.4, 207.6. HRMS-ESI (m/z) $[M + Na]^+$ calcd for $C_{18}H_{33}NO_3Si$ 362.21219, found 362.21228.

(*R*)-Trideca-3,4-dien-1-ol (18). To a cooled (0 °C) solution of **11f** (53 mg, 0.159 mmol) in EtOH (3.2 mL) was added *n*-Bu_4NF solution (1.0 M in THF, 159 μL, 0.159 mmol). After being stirred for 2 min, the mixture was concentrated and filtered through a pad of silica gel (3 mg) using Et_2O/hexane (1:1). The mixture was concentrated to give an inseparable mixture of **17** and ethyl (2*E*,4*E*)-trideca-2,4-dienoate (1.0:0.6, 29.2 mg), which was used in the next step without purification.

To a cooled (0 °C) suspension of $LiAlH_4$ (4.6 mg, 0.122 mmol) in THF (1.0 mL) was added a solution of the above compound in THF (1.0 mL). After the mixture was stirred at the same temperature for 30 min, a few drops of water were added. The mixture was diluted with 1% HCl (5 mL) and extracted with Et_2O (5 mL × 3). The combined organic phases were washed with saturated aqueous $NaHCO_3$ (5 mL) and saturated brine (5 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 3 g, elution with hexane/Et_2O = 2:1) to give **18** with inseparable allyl alcohol originated from ethyl (2*E*,4*E*)-trideca-2,4-dienoate (7.8 mg).

To remove the allyl alcohol, the solution of above mixture in CH_2Cl_2 (2 mL) was treated with MnO_2 (7 mg) for 2 h. The mixture was filtered through a pad of Celite and concentrated. The residual oil was subjected to column chromatography (silica gel, 2 g, elution with hexane/Et_2O = 3:1) to give **18** (5.2 mg, 15%, 3 steps) as a colorless oil: $[\alpha]_D^{23}$ −24.7 (*c* 0.260, Et_2O).

(*R*,2*E*,4*Z*)-4-Bromo-1-(*tert*-butyldimethylsilyl)trideca-2,4-dien-1-ol (21). To a cooled (−80 °C) solution of **9f** (100 mg, 0.258 mmol) in toluene (0.7 mL) was added dropwise a solution of chiral lithium amide **20** generated from (S)-2,2-dimethyl-*N*-(2-(4-methylpiperazin-1-yl)-1-phenylethyl)propan-1-amine (89.7 mg, 0.310 mmol) and MeLi−LiBr (0.86 M in Et_2O, 360 μL, 0.310 mmol) in toluene (1.54 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 15 min before the addition of a solution of AcOH (0.5 M in toluene, 0.325 mmol) was added. The mixture was diluted with hydrochloric acid (1%, 10 mL) and extracted with Et_2O (10 mL × 3). The combined organic phases were successively washed with saturated NH_4Cl (15 mL) and saturated brine (15 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 5 g, elution with hexane/Et_2O = 19:1) to give (*R*)-**21** (74.2 mg, 76%, er >99:1) as a pale yellow oil: R_f = 0.19 (hexane/Et_2O = 19:1); $[\alpha]_D^{21}$ +19.7 (*c* 0.720, $CHCl_3$), Chiralcel OD-H (25 cm), hexane/EtOH (1000:1), flow rate 1.0 mL/min, detection at 254 nm, t_R = 16.6 min (major) and 19.5 min (minor); IR (NaCl) 2952, 2927, 2857, 1689, 1628, 1553 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.01 (3H, s), 0.02 (3H, s), 0.88 (3H, t, *J* = 7.1 Hz), 0.96 (9H, s), 1.27−1.29 (10H, m), 1.40−1.50 (2H, m), 2.28 (2H, dt, *J* = 7.6, 7.3 Hz), 4.32 (1H, d, *J* = 5.2 Hz), 5.87 (1H, t, *J* = 7.3 Hz), 6.12 (1H, d, *J* = 14.6 Hz), 6.25 (1H, dd, *J* = 14.6, 5.2 Hz); ^{13}C NMR ($CDCl_3$) δ −8.7, −7.4, 14.3, 17.3, 22.9, 27.1, 28.7, 29.4, 29.5, 29.6, 31.8, 32.1, 66.7, 124.3, 124.7, 132.5, 136.8; HRMS-ESI (*m*/*z*) [M - H]$^+$ calcd for $C_{19}H_{37}BrOSi$ 387.17133, found 387.17136.

Determination of Absolute Configuration of 21 (Modified Mosher Method). To solution of (*R*)-(+)-MTPA (91.7 mg, 0.392 mmol) and $(COCl)_2$ (158 μL, 1.253 mmol) in hexane (4.3 mL) was added DMF (30 μL, 0.392 mmol). After being stirred at room temperature for 30 min, the mixture was filtrated and concentrated. Excess $(COCl)_2$ was removed by repeated azeotropic distillation with hexane, and a solution of **21** (61.0 mg, 0.157 mmol), Et_3N (175 μL, 1.253 mmol), and DMAP (19.1 mg, 0.157 mmol) in a minimum amount of CH_2Cl_2 (few drops) and hexane (3.6 mL) was added to the mixture. After being stirred at room temperature for 5 min, the mixture was diluted with saturated $NaHCO_3$ solution (15 mL) and extracted with EtOAc (15 mL × 2). The combined organic phases were washed with saturated brine (15 mL), dried, and concentrated. The residual oil was passed through a pad of silica gel (1g, elution with CH_2Cl_2), and the resulting crude oil was subjected to column chromatography (silica gel 5 g, elution with hexane/Et_2O = 29:1) to give (*R*, *R*)-**25** (33.8 mg, 37%) as a pale yellow oil and recover the starting material **9f** (14.4 mg, 24%): R_f = 0.32 (hexane/Et_2O = 29:1); $[\alpha]^{23}_D$ +54.23 (*c* 1.08, CH_2Cl_2); IR (NaCl) 2928, 2857, 1748, 1636, 1557 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.03 (3H, s), −0.00 (3H, s), 0.86 (9H, s), 0.87−0.90 (3H, m), 1.23−1.30 (10H, m), 1.40−1.49 (2H, m), 2.28 (2H, td, *J* = 7.1, 7.1 Hz), 3.54 (3H, s), 5.64 (1H, d, *J* = 7.3 Hz), 5.81 (1H, t, *J* = 7.1 Hz), 5.99 (1H, d, *J* = 14.9 Hz), 6.09 (1H, dd, *J* = 14.9, 7.3 Hz), 7.35−7.41 (3H, m), 7.51−7.53 (2H, m); ^{13}C NMR ($CDCl_3$) δ −7.8, −7.6, 14.3, 17.0, 22.9, 26.9, 28.6, 29.4, 29.5, 29.6, 31.8, 32.0, 55.6, 71.2, 84.7 (q, J_{C-F} = 27.8 Hz), 123.7 (d, J_{C-F} = 288.9 Hz), 124.4, 127.7, 128.6, 128.8, 129.7, 130.0, 132.6, 134.8; HRMS-ESI (*m*/*z*) [M + Na]$^+$ calcd for $C_{29}H_{44}BrF_3O_3Si$ 627.20874, found 627.20935.

To solution of (*S*)-(+)-MTPA (107.5 mg, 0.459 mmol) and $(COCl)_2$ (186 μL, 1.469 mmol) in hexane (5 mL) was added DMF (35.5 μL, 0.459 mmol). After being stirred at room temperature for 30 min, the mixture was filtrated and concentrated. Excess $(COCl)_2$ was removed by repeated azeotropic distillation with hexane, and a solution of **21** (71.5 mg, 0.184 mmol), Et_3N (204 μL, 1.469 mmol), and DMAP (22.4 mg, 0.184 mmol) in a minimum amount of CH_2Cl_2 (few drops) and hexane (4 mL) was added to the mixture. After being stirred at room temperature for 5 min, the mixture was diluted with saturated $NaHCO_3$ solution (15 mL) and extracted with EtOAc (15 mL × 2). The combined organic phases were washed with saturated brine (15 mL), dried, and concentrated. The residual oil was passed through a pad of silica gel (1g, elution with CH_2Cl_2), and the resulting crude oil was subjected to column chromatography (silica gel 5 g, elution with hexane/Et_2O = 39:1) to give (*S*,*R*)-**25** (50.9 mg, 49%) as a pale yellow oil: R_f = 0.24 (hexane/Et_2O = 39:1); $[\alpha]^{24}_D$ +27.31 (*c* 1.00, CH_2Cl_2); IR (NaCl) 2952, 2928, 2857, 1748, 1637, 1607, 1557, 1534 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.01 (3H, s), 0.03 (3H, s), 0.90 (9H, s), 0.89 (3H, t, *J* = 7.1 Hz), 1.27−1.30 (10H, m), 1.39−1.44 (2H, m), 2.26 (2H, td, *J* = 7.1, 7.1 Hz), 3.53 (3H, s), 5.58 (1H, d, *J* = 6.8 Hz), 5.71 (1H, t, *J* = 7.1 Hz), 5.84 (1H, d, *J* = 14.9 Hz), 6.04 (1H, dd, *J* = 14.9, 6.8 Hz), 7.37−7.42 (3H, m), 7.50−7.52 (2H, m); ^{13}C NMR ($CDCl_3$) δ −7.6, −7.4, 14.3, 17.1, 22.9, 26.9, 28.6, 29.4, 29.5, 29.6, 31.8, 32.1, 55.7, 70.9, 85.0 (q, J_{C-F} = 27.8 Hz), 123.6 (d, J_{C-F} = 287.9 Hz), 124.5, 127.8, 127.8, 128.6, 129.7, 130.2, 132.3, 134.3, 166.7; HRMS-ESI (*m*/*z*) [M + Na]$^+$ calcd for $C_{29}H_{44}BrF_3O_3Si$ 627.20874, found 627.20941.

(*R*,*Z*)-*tert*-Butyldimethyl(trideca-1,3,4-trien-1-yloxy)silane (23). To a cooled (−80 °C) solution of **9f** (80.0 mg, 0.207 mmol) in toluene (0.5 mL) was added dropwise a solution of chiral lithium amide **20** generated from (*S*)-2,2-dimethyl-*N*-(2-(4-methylpiperazin-1-yl)-1-phenylethyl)propan-1-amine (71.7 mg, 0.248 mmol) and MeLi−LiBr (0.86 M in Et_2O, 288 μL, 0.248 mmol) in toluene (1.2 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 15 min, and then THF (1.0 mL) was added. The mixture was allowed to warm to −20 °C over 30 min. A solution of AcOH (1.0 M in THF, 0.250 mmol) was added. The mixture was diluted with hydrochloric acid (1%, 10 mL) and extracted with Et_2O (15 mL × 3). The combined organic phases were successively washed with saturated NH_4Cl (15 mL) and saturated brine (15 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 5 g, elution with hexane) to give **23** (47.7 mg, 78%, (*R*)-**23**:(*S*)-**23** = 65:35, Chiralcel OD-H (25 cm × 2), hexane, flow rate 0.3 mL/min, detection at 254 nm, t_R = 22.9 min (minor, *S* isomer) and 24.5 min (major, *R* isomer)). as a pale yellow oil and (*R*)-**21** (6.0 mg, 8%, er >99:1) as a pale yellow oil.

Determination of Absolute Configuration of 23. To a cooled (−80 °C) solution of the chiral lithium amide **20**, generated from (*S*)-2,2-dimethyl-*N*-(2-(4-methylpiperazin-1-yl)-1-phenylethyl)propan-1-amine and MeLi−LiBr (0.98 M in Et_2O, 295 μL, 0.289 mmol) in toluene (0.9 mL) at 0 °C, was added dropwise a solution of the (*E*)-1-(*tert*-butyldimethylsilyl)tetradec-2-en-4-yn-1-one (73.8 mg, 0.241 mmol) in toluene (0.6 mL). The reaction mixture was stirred at the same temperature for 30 min before the addition of a solution of *t*-BuOH (27 μL, 0.289 mmol) in THF (0.9 mL). After being allowed to warm to −20 °C over 10 min, the mixture was quenched by the addition of AcOH (0.5 M in THF, 0.580 mmol). The mixture was diluted with hydrochloric acid (1%, 10 mL) and extracted with Et_2O (10 mL × 3). The combined organic phases were successively washed with saturated aqueous $NaHCO_3$ solution (5 mL) and saturated brine (5 mL), dried, and concentrated. The residual oil was subjected to flash column chromatography (silica gel, 5 g, elution with hexane/Et_2O = 50:1, contained 3% Et_3N) to give **23** (52.9 mg, 71%, 92:8 er)

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as a colorless oil: $[\alpha]^{23}_{D}$ +14.7 (*c* 1.40, CH_2Cl_2) (er = 94:6); IR (NaCl) 3444, 2955, 2928, 2857, 1963, 1700, 1639 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.15 (6H, s), 0.82 (3H, t, *J* = 6.6 Hz), 0.94 (9H, s), 1.27−1.34 (10H, m), 1.38−1.43 (2H, m), 2.00 (2H, tdd, *J* = 6.9, 6.9, 3.0 Hz), 4.98 (1H, dd, *J* = 10.5, 5.7 Hz), 5.26 (1H, dt, *J* = 6.9, 6.9 Hz), 6.16 (1H, ddd, *J* = 5.7, 1.4, 1.4 Hz), 6.17−6.22 (1H, m); ^{13}C NMR ($CDCl_3$) δ −5.2, −5.2, 14.3, 18.5, 22.9, 25.8, 29.2, 29.3, 29.4, 29.5, 29.6, 32.1, 87.2, 92.1, 106.3, 139.2, 206.2; HRMS-APCI (*m*/*z*) $[M - H]^+$ calcd for $C_{19}H_{36}OSi$ 307.2452, found 307.2452.

To a cooled (ice−water) solution of above compound (58.5 mg, 0.19 mmol, 92:8 er) and K_2CO_3 (31.4 mg, 0.23 mmol) in Et_2O (0.95 mL) and H_2O (0.95 mL) was added *m*-CPBA (77%, 42.5 mg, 0.19 mmol). After being allowed to warm to room temperature over 1 h, the reaction mixture was diluted with saturated 20% aqueous K_2CO_3 solution (10 mL) and extracted with Et_2O (10 mL × 3). The combined organic phases were washed with 20% aqueous K_2CO_3 solution (10 mL) and saturated brine (10 mL), dried, and concentrated. The residual oil was used in the next step without purification.

To a cooled (−80 °C) solution of the above compound in THF (1.5 mL) was added a solution of TBAF (0.35 M in THF−EtOH (5:9), 356 mL, 0.20 mmol). The reaction mixture was allowed to warm to 0 °C over 20 min, and then $NaBH_4$ (8.3 mg, 0.22 mmol) was added to the solution. After being stirred at the same temperature for 30 min, the reaction mixture was diluted with saturated aqueous NH_4Cl solution (10 mL) and extracted with Et_2O (10 mL × 3). The combined organic phases were washed with H_2O (10 mL) and saturated brine (10 mL), dried, and concentrated. The residual oil was used in the next step without purification.

To a cooled (ice−water) solution of above compound in Et_2O (0.66 mL) was added H_5IO_6 (19.5 mg, 86 μmol). After being stirred at room temperature for 30 min, the mixture was filtered through a plug of Celite and concentrated. The residual oil was used in the next step without purification.

To a cooled (ice−water) suspension of NaH (60%, 3.7 mg, 92 μmol) in THF (0.7 mL) was added HWE reagent (16 μL, 99 μmol). The reaction mixture was allowed to warm to room temperature and stirred for 10 min. The mixture was cooled to 0 °C, and then the above compound in THF (0.6 mL) was added. After being stirred at room temperature for 30 min, the reaction mixture was diluted with H_2O (5 mL) and extracted with Et_2O (5 mL × 3). The combined organic phases were washed with H_2O (5 mL) and saturated brine (5 mL), dried, and concentrated. The residual oil was subjected to flash column chromatography (silica gel, 5 g; elution with hexane/Et_2O = 30:1) to give methyl 2,4,5-tetradecatrienoate (4.1 mg, 9% overall yield). $[\alpha]^{26}_{D}$ −97.4 (*c* = 0.21, hexane) (er = 86:14); Chiralpak AS3 (25 cm), hexane/*i*-PrOH = 200:1, flow rate 0.40 mL/min, detection at 254 nm, t_R = 11.1 min (major) and 14.3 min (minor), er = 82:18.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and ^{13}C NMR spectra, chiral HPLC analyses data, computational details, and additional schemes of the experiments for determination of configuration of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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NOTE ADDED AFTER ASAP PUBLICATION

The solvents in entries 2 and 3 of Table 1 were corrected on December 9, 2014.