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# An Efficient Method for the Optical Resolution of 3-Hydroxy-2-substituted-4-alkynoates: A Highly Stereoselective Total Synthesis of (+)-Bengamide E[1]

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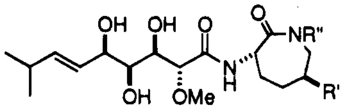
A novel procedure for the optical resolution of 3-hydroxy-2-substituted-4-alkynoates and its application to the stereoselective total synthesis of (+)-bengamide E are described. 3-Hydroxy-2-substituted-4-alkynoates, derived from the aldol reaction of cobalt-complexed propynals with ketene *O*-silyl *O*,*S*-acetals, were easily resolved by the formation of a chiral carbamate followed by cobalt complexation. Chiral 2-(benzyloxy)-3-hydroxy-4-alkynoate derivatives thus obtained were used as starting materials for a highly stereoselective total synthesis of (+)-bengamide E.

## Introduction

Recent efforts from our[2] and other laboratories[3] have revealed that the aldol reaction of cobalt-complexed propynal **1** with *O*-silyl enol ethers under Mukaiyama conditions,[4] followed by decomplexation, affords *syn*-aldol condensation products in a highly stereoselective manner. Ketene *O*-silyl *O*,*S*-acetals **3** bearing unbranched alkyl substituents such as methyl,[5] ethyl,[5] and *n*-butyl[6] groups have also been found to be excellent silyl nucleophiles, leading to the exclusive formation of the *syn*-isomer **4** regardless of the geometry of **3** in the aldol reaction. In addition to these novel *syn*-selective reactions, we have developed a highly *anti*-selective aldol reaction[5,6] by using propynal **2**, the parent aldehyde of cobalt complex **1**, in the presence of a Lewis acid to form the corresponding *anti*-product **5** (Scheme 1). These stereoselective as well as stereocomplementary reactions have been successfully applied to total syntheses of (±)-PS-5,[5] (±)-6-*epi*-PS-5,[5] and (±)-blastmycinone and its three diastereoisomers.[6] In this paper, (+)-bengamide E (**10**), a stereochemically more complex natural product, has been targeted in order to demonstrate the potential of our newly developed stereoselective aldol reaction in the synthesis of natural products. We describe herein a highly stereoselective total synthesis of (+)-bengamide E based on (i) a *syn*-selective aldol reaction of cobalt-complexed propynal and (ii) a novel procedure for the optical resolution of a 2-(benzyloxy)-3-hydroxy-4-alkynoate derivative.



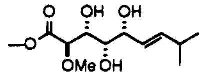
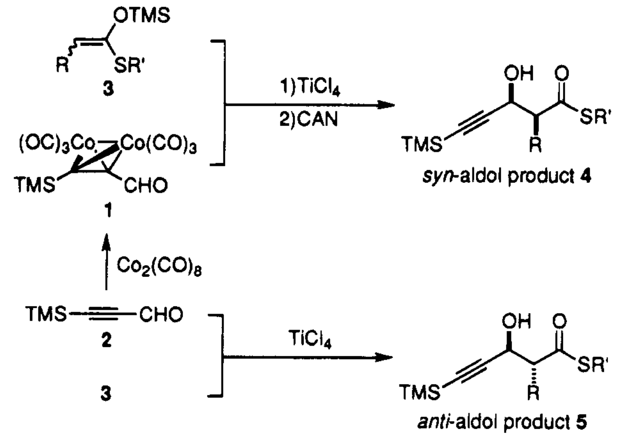
| | R' | R" |
|---|---|---|
| Bengamide A (**6**) | OCO(CH$_2$)$_{12}$CH$_3$ | H |
| B (**7**) | | Me |
| C (**8**) |  | H |
| D (**9**) | | Me |
| E (**10**) | H | H |
| F (**11**) | | Me |

**Figure 1.**

**Scheme 1**



Bengamides A–F (**6–11**)[7] were isolated from a Choristid sponge collected in the Fiji Islands (Figure 1). Bengamides A and B have been shown to possess significant antihelminthic activity as well as cytotoxicity. Their structures and absolute configurations have been well established by spectroscopic analysis and chemical transformation. The (2*R*,3*R*,4*S*,5*R*,6*E*)-3,4,5-trihydroxy-2-methoxy-8-methyl-6-nonenyl side chain (C-10 side chain) was identified as a common structural feature of the bengamide family. Therefore, a stereoselective construction of the C-10 side chain involving the four contiguous stereogenic centers and the double bond would be the most crucial points in developing a general procedure for the total synthesis of the bengamide family. Several groups have already attained total syntheses of benga-

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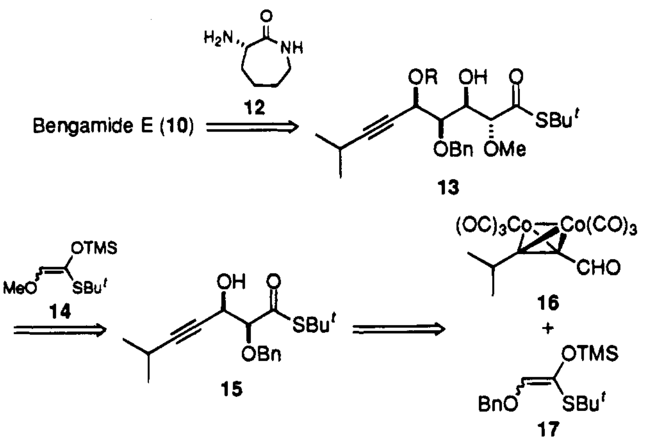
Scheme 2



mide E,[8] B,[8b,9] and A,[10] as well as the C-10 side chain,[11] starting from natural resources like cyclitol,[8a,9,10] glucose,[8b,c,11] tartaric acid,[8d] and glyceraldehyde.[8e]

## Results and Discussion

**Retrosynthetic Analysis of (+)-Bengamide E.** Scheme 2 illustrates our strategy for a synthesis of (+)-bengamide E (**10**), which involves dual highly stereoselective aldol reactions starting from the cobalt complex **16**. It was predicted that an aldol reaction of complex **16** with ketene *O*-silyl *O*,*S*-acetal **17** possessing an oxygen functionality at the vinylic position would afford the *syn*-aldol condensation product **15** in a highly stereoselective manner based on our previous observations.[5,6] By taking advantage of the hydroxy functionality at the α-stereogenic center of the aldol product **15**, we expected that the second aldol reaction with *O*,*S*-acetal **14** under chelation-controlled conditions[12] might selectively provide the 2,3-*anti*-3,4-*syn*-product **13**, which corresponds to the framework of the C-10 side chain with the proper stereochemistry. Coupling of **13** with commercially available (*S*)-2-aminocaprolactam (**12**), followed by some chemical modifications of the side chain, would lead to (+)-bengamide E (**10**). According to the above strategy, the C-10 side chain moiety should not be racemic, but optically active with high enantiomeric purity. Because this strategy would suffer from the production of an undesired diastereoisomer at the penultimate coupling step if a racemic C-10 side chain was employed, it seemed reasonable to produce the optically pure side chain by optical resolution prior to exposing it to the amide formation reaction.

**Development of the Method for Optical Resolution of Aldol Products.** Pirkle[13,14] has reported some examples of optical resolution of various propynyl alcohols employing optically active 1-(1-naphthyl)ethyl isocyanate. It was shown that condensation of racemic propynyl alcohols with chiral 1-(1-naphthyl)ethyl isocyanate proceeds efficiently to yield a mixture of two diastereoisomers of the carbamates which are easily separated by silica gel chromatography. Thus, our first interest was in examining whether Pirkle's procedure could be applicable to our aldol products.

2-Alkyl-3-hydroxy-4-alkynoates, **4a**,[5] **4b**[6] (*syn*-aldol products), and **5a**[5] (*anti*-aldol product) were chosen as substrates for optical resolution (Scheme 3). A mixture of **4a** and (*S*)-1-phenylethyl isocyanate (**18**) was heated at 60 °C for 8 h in the presence of *N*,*N*-dimethyl-2-aminoethanol to provide the corresponding carbamates **20** and **21**, which unexpectedly could hardly be differentiated by their chromatographic behavior. We imagined that enhancement of the bulkiness of the triple bond next to the crucial chrial center would help to differentiate the chromatographic behavior of these two diastereoisomers on the basis of Mioskowski's report.[15] Thus, the mixture of carbamates **20** and **21** was treated with dicobalt octacarbonyl [$Co_2(CO)_8$] to yield the corresponding two cobalt-complexed diastereomeric compounds, the chromatographic behaviors of which were fortunately quite different. The two cobalt-complexed carbamates were easily isolated by column chromatography and subsequently treated with CAN in methanol to give chiral carbamates **20** [$[\alpha]^{24}_{D}$ −45.0° (*c* 0.50, $CHCl_3$)] and **21** [$[\alpha]^{24}_{D}$ −19.4° (*c* 0.50, $CHCl_3$)]. The chiral auxiliaries of **20** and **21** were removed by $HSiCl_3$[14] in benzene to furnish the chiral aldol products (+)-**4a** [$[\alpha]^{22}_{D}$ +44.8° (*c* 0.51, $CHCl_3$)] and (−)-**4a** [$[\alpha]^{22}_{D}$ −44.2° (*c* 0.50, $CHCl_3$)], respectively. Variance of the chiral auxiliary from (*S*)-1-phenylethyl isocyanate (**18**) to (*R*)-1-(1-naphthyl)ethyl isocyanate (**19**) did not affect the ease of separation of the diastereomeric carbamates **22** [$[\alpha]^{25}_{D}$ +18.4° (*c* 0.50, $CHCl_3$)] and **23** [$[\alpha]^{25}_{D}$ −16.9° (*c* 0.50, $CHCl_3$)]. In addition, the corresponding *anti*-aldol product **5a** and the α-butyl congener (*syn*-aldol product) **4b** could be easily resolved by the procedure described for **4a** (see Experimental Section).

Although the absolute stereochemistry of these resolved products was not clear at this point, we developed an efficient and convenient two-step procedure for the optical resolution of 2-alkyl-3-hydroxy-4-alkynoates involving (i) chiral carbamate formation with 1-phenylethyl isocyanate or 1-(1-naphthyl)ethyl isocyanate and (ii) cobalt complexation.

**Total Synthesis of Bengamide E.** Our next concern was what level of stereoselectivity might be achieved in the aldol reaction of cobalt complex **16** with ketene *O*-silyl *O*,*S*-acetal **17** (Scheme 4). The cobalt complex **16** was easily synthesized from 4-methyl-2-pentyn-1-ol (**32**)[16] by successive PCC oxidation and cobalt complexation with $Co_2(CO)_8$. The *O*,*S*-acetal **17** was prepared from *S*-*tert*-butyl (benzyloxy)ethanethioate (**33**) according to Gennari's procedure.[12] The ratio of (*E*)- to (*Z*)-isomers of **17** was determined to be 73:27 by analysis of its $^1H$ NMR spectrum based on the literature precedent.[17] The aldol reaction of complex **16** with *O*,*S*-acetal **17** in the presence of $BF_3{\cdot}OEt_2$ in dry $CH_2Cl_2$ at −78 °C provided the aldol condensation products with cobalt complexation, which

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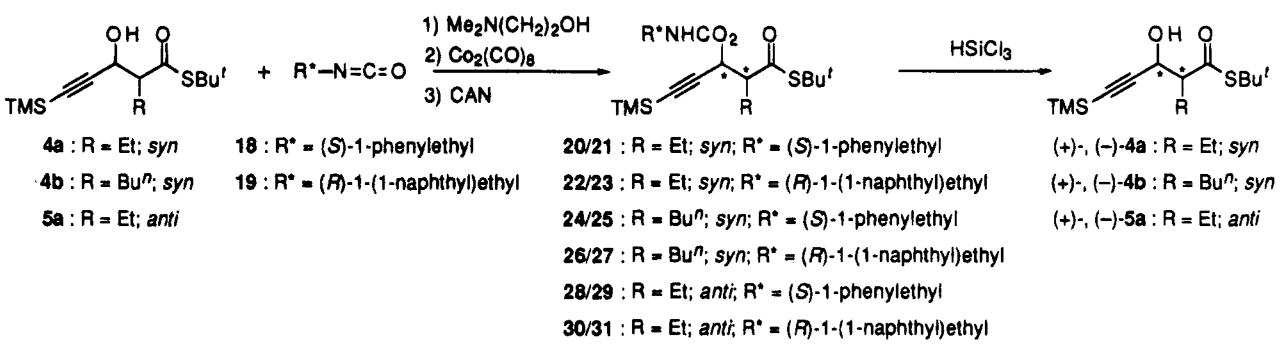
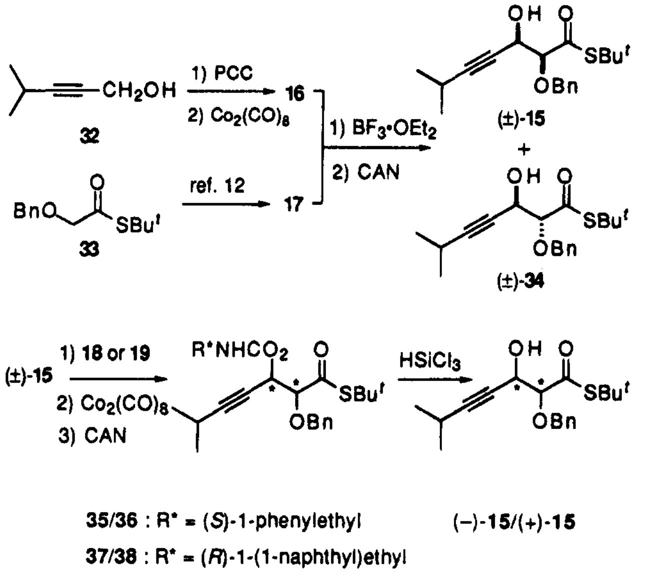
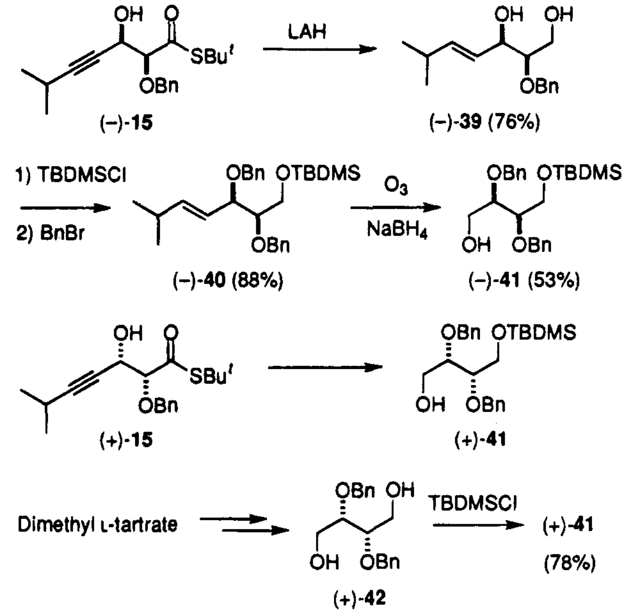
**Scheme 3**



**Scheme 4**



**Scheme 5**



were subsequently decomplexed with CAN in methanol at 0 °C to give the *syn*-isomer (±)-**15** along with a small amount of the *anti*-isomer (±)-**34** [89%, (±)-**15**/(±)-**34** = 95/5][18] as expected.[2,5,6] It is noteworthy that a mixture of **15** and **34** as well as considerable amounts of their debenzylated derivatives were obtained when $TiCl_4$[5,6] was used instead of $BF_3{\cdot}OEt_2$ in the above aldol reaction.

We have already reported a highly *syn*-selective aldol reaction[5,6] of cobalt-complexed propynal **1** (with ketene *O*-silyl *O,S*-acetals **3** (R = unbranched alkyl substituent). Since aldol condensation of complex **16** with *O,S*-acetal **17** gave the *syn*-product **15** in a highly stereoselective manner, we can now add another successful example to our collection of stereoselective aldol reactions of the (propynal)$Co_2(CO)_6$ complex. Oxygen functionality at the $C_2$-position of *O,S*-acetals was tolerated under the aldol conditions we used in a series of aldol reactions of cobalt-complexed propynals **1**.

With racemic *syn*-aldol adduct (±)-**15** in hand, we set about its optical resolution. Reaction of (±)-**15** with (*S*)-1-phenylethyl isocyanate (**18**) according to the aforementioned procedure gave an inseparable mixture of **35** and **36**, which was subsequently converted into a mixture of the corresponding cobalt-complexed compounds by treatment with $Co_2(CO)_8$. Chromatographic separation followed by demetallation with CAN afforded the carbamates (+)-**35** $[[\alpha]^{27}_D$ +58.2° (*c* 0.50, $CHCl_3$)] and (−)-**36** $[[\alpha]^{27}_D$ −111° (*c* 0.50, $CHCl_3$)], respectively. Removal of the carbamate moiety of (+)-**35** was realized by the procedure described for conversion of (−)-**20** into (+)-**4a** to furnish (−)-**15** $[[\alpha]^{24}_D$ −87.1° (*c* 0.50, $CHCl_3$)] in 30% overall yield from (±)-**15**. The antipode, (+)-**15** $[[\alpha]^{24}_D$ +86.8° (*c* 0.50, $CHCl_3$)], was also obtained under the same conditions in 30% overall yield. Alternatively, (+)-**15** $[[\alpha]^{23}_D$ +86.6° (*c* 1.0, $CHCl_3$)] and (−)-**15** $[[\alpha]^{23}_D$ −86.7° (*c* 1.0, $CHCl_3$)] could also be obtained in 23 and 25% overall yield through the corresponding carbamates **37** and **38**, respectively, when (*R*)-1-(1-naphthyl)ethyl isocyanate (**19**) was employed instead of (*S*)-1-phenylethyl isocyanate (**18**). Cobalt complexation of the carbamates **35**/**36** and **37**/**38** enabled us to isolate each enantiomer by chromatography without any difficulties. $^1H$ NMR spectral analysis of (−)- and (+)-**15** in the presence of tris-[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]-europium(III) in $CDCl_3$ indicated that each isomer was free from contamination with its antipode. We attempted the optical resolution of cobalt-complexed (±)-**15** directly, without initial decomplexation, by using **18** or **19**. However, no carbamate formation could be observed under several sets of conditions, presumably due to the bulkiness of the cobalt-complexed triple bond moiety.

The absolute configuration of the *syn*-aldol products (−)- and (+)-**15** were determined (Scheme 5) by independent chemical transformations. Reduction of (−)-**15** with lithium aluminum hydride (LAH) afforded diol (−)-**39** $[[\alpha]^{23}_D$ −14.5° (*c* 0.50, $CHCl_3$)] in 76% yield. Selective monosilylation of the primary hydroxy group[19] followed

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(18) The ratio was determined by $^1H$ NMR spectroscopy.

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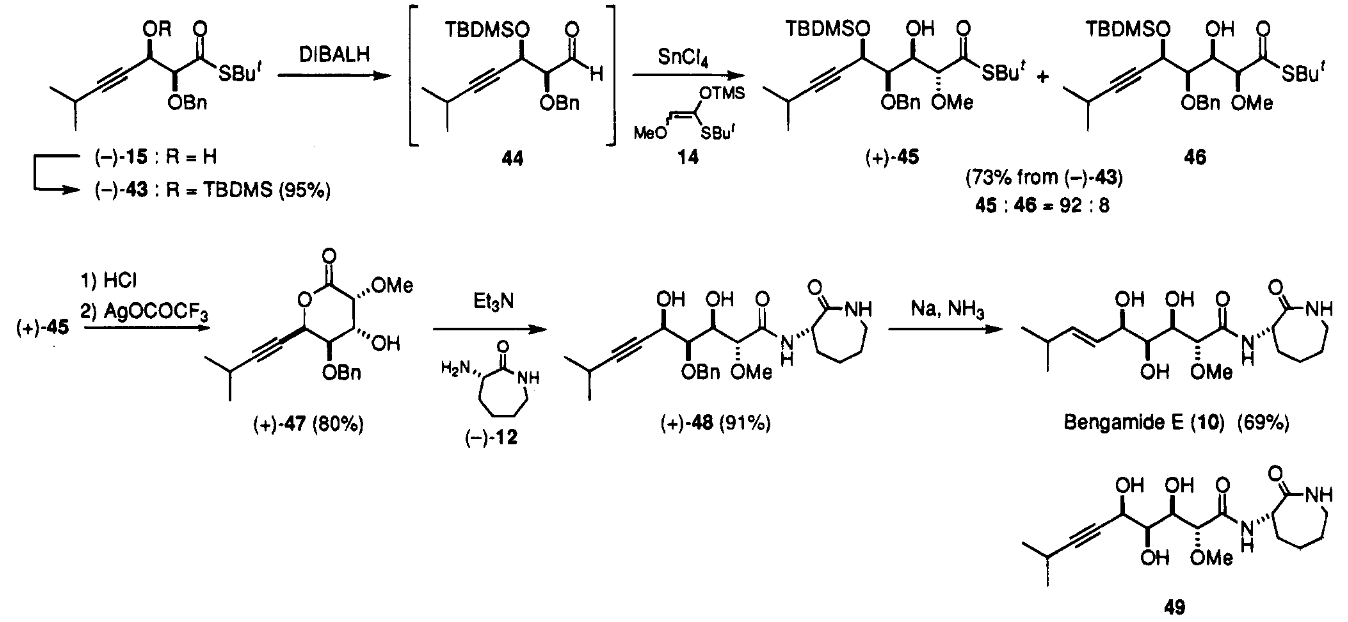
Scheme 6



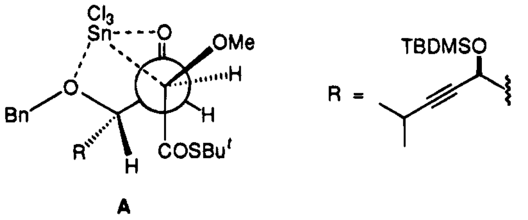


**Figure 2.**

by benzylation of the allylic free hydroxy group provided (−)-**40** [$[\alpha]^{18}_{\mathrm{D}}$ −25.3° (*c* 0.53, $CHCl_3$), 88%], which after ozonolysis and subsequent reductive workup produced alcohol (−)-**41** [$[\alpha]^{22}_{\mathrm{D}}$ −14.4° (*c* 0.50, $CHCl_3$)] in 53% yield. Similar sequences were applied to the antipode (+)-**15** to afford alcohol (+)-**41** [$[\alpha]^{22}_{\mathrm{D}}$ +13.9° (*c* 0.50, $CHCl_3$)]. The authentic sample of (+)-**41** [$[\alpha]^{17}_{\mathrm{D}}$ +13.3° (*c* 0.50, $CHCl_3$), (lit.[20] $[\alpha]^{27}_{\mathrm{D}}$ +14.7° (*c* 0.95, $CHCl_3$)] was synthesized from dimethyl L-tartrate *via* the known 2,3-di-*O*-benzyl-L-threitol (**42**).[21] These transformations unambiguously established the absolute configuration of (+)-**15** as 2*R*,3*S* and (−)-**15** as 2*S*,3*R*.

With chiral *syn*-aldol product (−)-**15** in hand, the stage was set for elaboration to produce the C-10 side chain (Scheme 6). The β-hydroxy group of (−)-**15** was protected with TBDMSCl to furnish (−)-**43** [$[\alpha]^{27}_{\mathrm{D}}$ −95.8° (*c* 0.50, $CHCl_3$), 95%]. Reduction of (−)-**43** with DIBALH afforded aldehyde **44**, which was immediately exposed to an aldol reaction under chelation-controlled conditions with stannyl *C*-enolate,[12,22] prepared *in situ* from ketene *O*-silyl *O*,*S*-acetal **14** (*E*/*Z* = 75/25)[18] and $SnCl_4$, to yield aldol product (+)-**45** [$[\alpha]^{27}_{\mathrm{D}}$ +30.9° (*c* 0.50, $CHCl_3$)] along with its 2-epimer **46** (**45**/**46** = 92/8)[18] in 73% overall yield from **43**. The highly stereoselective formation of (+)-**45** may be interpreted in terms of the chelation-controlled transition state (**A**) depicted in Figure 2 according to Gennari's model.[12,22] This stereoselective aldol reaction furnished the carbon framework required for the synthesis of the C-10 side chain of bengamides with the correct stereochemistry.

The next phase of our synthesis of (+)-bengamide E involved some modifications of (+)-**45** and coupling with the cyclic lysine derivative (−)-**12**. Prior to coupling with cyclic lysine derivative (−)-**12**, the aldol product (+)-**45** was transformed into the corresponding δ-lactone (+)-**47** [$[\alpha]^{25}_{\mathrm{D}}$ +93.9° (*c* 0.50, $CHCl_3$] in 80% yield by hydrolysis with hydrochloric acid and lactone formation with silver(I) trifluoroacetate.[23] The coupling of (+)-**47** with (*S*)-α-amino-ε-caprolactam [(−)-**12**] proceeded in the presence of triethylamine in THF−dioxane (10:1), without protection of the $C_3$-hydroxy group, to give the condensation product (+)-**48** [$[\alpha]^{23}_{\mathrm{D}}$ +28.1° (*c* 0.26, $CHCl_3$)] in 91% yield. Although direct transformation of (+)-**45** into (+)-**48** with silver(I) trifluoroacetate was examined, amide bond formation did not occur and the starting (+)-**45** was recovered intact. Birch reduction ($Na/NH_3$) of (+)-**48** effected simultaneous removal of the benzyl group on the $C_4$-hydroxy group of the side chain as well as reduction of the triple bond to a *trans*-double bond to provide (+)-bengamide E (**10**) [$[\alpha]^{22}_{\mathrm{D}}$ +24° (*c* 0.1, MeOH) (lit.[8a] $[\alpha]^{29}_{\mathrm{D}}$ +25° (*c* 0.29, MeOH)] in 69% yield. This final step was somewhat capricious and the alkyne derivative **49**, a presumed intermediate in the conversion of **48** to **10**, could sometimes be detected as a byproduct. However, this is not a serious drawback, because rereduction of a mixture of **10** and **49** under the same conditions gave pure **10** in 62−69% overall yield from (+)-**48**. Synthetic (+)-bengamide E proved to be identical with an authentic specimen[8a] by comparison with $^1H$ and $^{13}C$ NMR spectra and specific rotation.

## Conclusion

We have developed a novel procedure for the optical resolution of 3-hydroxy-2-substituted-4-alkynoates through consecutive formation of a chiral carbamate with (*S*)-1-phenylethyl isocyanate or (*R*)-1-(1-naphthyl)ethyl isocyanate and cobalt complexation. A highly stereoselective total synthesis of (+)-bengamide E was completed using

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a newly developed *syn*-selective aldol reaction as well as a novel optical resolution.

## Experimental Section

Melting points are uncorrected. IR spectra were measured in $CHCl_3$. $^1$H NMR spectra were taken in $CDCl_3$. $CHCl_3$ (7.26 ppm) was used as an internal standard for silyl compounds without an aromatic group. TMS was employed as an internal standard for all other compounds. $^{13}$C NMR spectra were recorded in $CDCl_3$ with $CDCl_3$ (77.00 ppm) as an internal standard. $CH_2Cl_2$ was freshly distilled from phosphorus pentoxide and THF from sodium diphenyl ketyl, prior to use. Aldol reactions were performed in oven-dried glassware under an inert atmosphere of nitrogen. Silica gel (silica gel 60, 230−400 mesh, Nacalai Tesque) was used for chromatography. Organic extracts were dried over anhydrous $Na_2SO_4$. Ketene *O*-silyl *O*,*S*-acetals **14** and **17** were prepared according to Gennari's procedure.[20]

**General Procedure for Optical Resolution of Aldol Products.** A racemic aldol (1 equiv), an optically active isocyanate (2 equiv) and *N*,*N*-dimethyl-2-aminoethanol (0.05 mL/racemic aldol 1 mmol) were mixed and heated at 60 °C for 8 h. After the mixture was cooled to rt, the resulting white precipitate was filtered off by suction, and the filtrate was concentrated to dryness. The crude carbamates were added to a solution of $Co_2(CO)_8$ (1.5 equiv) in $CH_2Cl_2$ (5.0 mL/racemic aldol 1 mmol) under nitrogen at rt. After the mixture was stirred for 1 h, the $CH_2Cl_2$ was evaporated to leave an oil which was chromatographed with hexane−ethyl acetate (50:1) to give the cobalt-complexed carbamates. The carbamate was dissolved in methanol (5 mL/racemic aldol 1 mmol) to which CAN (4.2 equiv) was added portionwise at 0 °C. The reaction mixture was stirred for *ca.* 30 min (monitored by TLC), and the methanol was evaporated off. The residue was diluted with water and extracted three times with ethyl acetate. The combined extracts were washed successively with water and brine, dried, and evaporated to dryness. Chromatography of the residue with hexane−ethyl acetate (30:1) afforded the optically pure carbamates.

***S-tert*-Butyl (2*R*,3*R*)- and (2*S*,3*S*)-2-Ethyl-3-[[[(*S*)-1-phenylethyl]amino]carboxy]-5-(trimethylsilyl)-4-pentynethioates (20 and 21).** The carbamates **20** (143 mg, 38%) and **21** (148 mg, 39%) were obtained from racemic **4a** (250 mg, 0.87 mmol) and (*S*)-1-phenylethyl isocyanate (**18**, 255 mg, 1.73 mmol). The compound **20** was a colorless oil: $[\alpha]^{24}_D$ −45.0° (*c* 0.50, $CHCl_3$); MS *m/z* 434 ($M^+$ + 1, 1.2), 344 (19), 179 (77), 137 (29), 105 (100), 57 (11); IR 3450, 2170, 1725, 1680 cm$^{-1}$; $^1$H NMR $\delta$ 7.36−7.22 (m, 1H), 5.52 (d, 1H, $J$ = 7.3 Hz), 5.04 (d, 1H, $J$ = 5.9 Hz), 4.85 (quint, 1H, $J$ = 6.8 Hz), 2.73 (ddd, 1H, $J$ = 4.4, 7.3, 9.8 Hz), 1.80−1.58 (m, 2H), 1.49 (d, 3H, $J$ = 6.8 Hz), 1.44 (s, 9H), 0.92 (t, 3H, $J$ = 7.3 Hz), 0.17 (s, 9H); $^{13}$C NMR $\delta$ 199.1, 154.1, 143.3, 128.6, 127.3, 125.9, 100.7, 92.0, 65.1, 60.0, 50.8, 48.3, 29.7, 22.4, 21.9, 11.6, −0.3. Anal. Calcd for $C_{23}H_{35}NO_3SSi$: C, 63.70; H, 8.13; N, 3.23. Found: C, 63.85; H, 8.21; N, 3.23. The carbamate **21** was a colorless oil: $[\alpha]^{24}_D$ −19.4° (*c* 0.50, $CHCl_3$); MS *m/z* 434 ($M^+$ + 1, 0.9), 344 (12), 179 (49), 137 (25), 105 (80), 57 (100); IR 3450, 2170, 1725, 1680 cm$^{-1}$; $^1$H NMR $\delta$ 7.38−7.21 (m, 5H), 5.52 (d, 1H, $J$ = 6.8 Hz), 5.03 (d, 1H, $J$ = 6.3 Hz), 4.85 (quint, 1H, $J$ = 6.8 Hz), 2.81−2.64 (m, 1H), 1.85−1.57 (m, 2H), 1.48 (d, 3H, $J$ = 6.8 Hz), 1.47 (s, 9H), 0.96 (t, 3H, $J$ = 6.8 Hz), 0.15 (s, 9H); $^{13}$C NMR $\delta$ 199.3, 154.1, 143.1, 128.6, 127.4, 126.0, 100.7, 100.0, 65.1, 60.1, 50.8, 48.3, 40.7, 29.7, 21.9, 11.6, −0.3. Anal. Calcd for $C_{23}H_{35}NO_3SSi$: C, 63.70; H, 8.13; N, 3.23. Found: C, 63.92; H, 8.26; N, 3.19.

***S-tert*-Butyl (2*R*,3*R*)- and (2*S*,3*S*)-2-Ethyl-3-[[[(*R*)-1-(1-naphthyl)ethyl]amino]carboxy]-5-(trimethylsilyl)-4-pentynethioates (22 and 23).** Racemic aldol **4a** (209 mg, 0.73 mmol) and (*R*)-1-(1-naphthyl)ethyl isocyanate (**19**, 295 mg, 1.5 mmol) afforded the carbamates **22** (102 mg, 29%) and **23** (109 mg, 31%). Colorless solid product **22**: mp 119.0−119.5 °C (from ether); $[\alpha]^{25}_D$ + 18.4° (*c* 0.50, $CHCl_3$); MS *m/z* 483 ($M^+$, 0.7), 179 (99), 155 (100), 137 (42), 73 (43), 57 (99); IR 3450, 2170, 1725, 1675 cm$^{-1}$; $^1$H NMR $\delta$ 8.10 (d, 1H, $J$ = 8.8 Hz), 7.86 (d, 1H, $J$ = 7.3 Hz), 7.78 (d, 1H, $J$ = 8.3 Hz), 7.57−7.40 (m, 4H), 5.65 (quint, 1H, $J$ = 7.3 Hz), 5.57 (d, 1H, $J$ = 7.3 Hz), 5.11 (d, 1H, $J$ = 7.3 Hz), 2.71 (ddd, 1H, $J$ = 4.4, 7.3, 10 Hz), 1.80−1.52 (m, 2H), 1.66 (d, 3H, $J$ = 6.8 Hz), 1.41 (s, 9H), 0.90 (t, 3H, $J$ = 7.3 Hz), 0.18 (s, 9H); $^{13}$C NMR $\delta$ 199.1, 154.0, 138.5, 134.0, 130.8, 128.8, 128.2, 126.4, 125.7, 125.2, 123.3, 122.2, 100.8, 92.0, 65.1, 60.1, 48.3, 46.9, 29.7, 21.9, 21.6, 11.5, −0.3. Anal. Calcd for $C_{27}H_{37}NO_3SSi$: C, 67.04; H, 7.71; N, 2.90. Found: C, 67.25; H, 7.74; N, 2.76. Colorless solid product **23**: mp 136.5−137.0 °C (from ether); $[\alpha]^{25}_D$ −16.9° (*c* 0.50, $CHCl_3$); MS *m/z* 483 ($M^+$, 0.1), 179 (74), 155 (100), 137 (19), 73 (18), 57 (52); IR 3450, 2160, 1720, 1675 cm$^{-1}$; $^1$H NMR $\delta$ 8.12 (d, 1H, $J$ = 8.3 Hz), 7.86 (dd, 1H, $J$ = 1.0, 7.8 Hz), 7.79 (d, 1H, $J$ = 8.3 Hz), 7.58−7.42 (m, 4H), 5.71−5.61 (m, 1H), 5.55 (d, 1H, $J$ = 6.8 Hz), 5.08 (d, 1H, $J$ = 7.8 Hz), 2.81−2.67 (m, 1H), 1.83−1.34 (m, 2H), 1.66 (d, 3H, $J$ = 6.8 Hz), 1.47 (s, 9H), 0.96 (t, 3H, $J$ = 6.8 Hz), 0.14 (s, 9H); $^{13}$C NMR $\delta$ 199.3, 154.1, 138.3, 133.9, 130.9, 128.8, 128.3, 126.4, 125.8, 125.2, 123.3, 122.3, 100.7, 91.9, 65.2, 60.0, 48.4, 46.8, 29.7, 21.9, 21.5, 11.6, −0.3. Anal. Calcd for $C_{27}H_{37}NO_3SSi$: C, 67.04; H, 7.71; N, 2.90. Found: C, 66.75; H, 7.71; N, 2.79.

***S-tert*-Butyl (2*R*,3*R*)- and (2*S*,3*S*)-2-Butyl-3-[[[(*S*)-1-phenylethyl]amino]carboxy]-5-(trimethylsilyl)-4-pentynethioates (24 and 25).** The carbamates **24** (132 mg, 45%) and **25** (127 mg, 43%) were provided by treatment of **4b** (200 mg, 0.64 mmol) and **18** (234 mg, 1.6 mmol). Colorless solid **24**: mp 70.0−71.0 °C (from hexane); $[\alpha]^{27}_D$ −43.2° (*c* 0.50, $CHCl_3$); MS *m/z* 462 ($M^+$ + 1, 0.3), 372 (7.6), 240 (7.5), 207 (45), 165 (15), 105 (69), 73 (17), 57 (100); IR 3450, 2160, 1725, 1675 cm$^{-1}$; $^1$H NMR $\delta$ 7.35−7.22 (m, 5H), 5.53 (d, 1H, $J$ = 6.8 Hz), 4.98 (d, 1H, $J$ = 6.4 Hz), 4.86 (quint, 1H, $J$ = 6.8 Hz), 2.78 (ddd, 1H, $J$ = 4.4, 6.8, 9.8 Hz), 1.79−1.17 (m, 6H), 1.49 (d, 3H, $J$ = 7.3 Hz), 1.43 (s, 9H), 0.86 (t, 3H, $J$ = 6.8 Hz), 0.17 (s, 9H); $^{13}$C NMR $\delta$ 199.2, 154.0, 143.3, 128.6, 127.3, 125.9, 100.7, 92.0, 65.2, 58.3, 50.7, 48.3, 29.7, 29.1, 28.1, 22.5, 22.4, 13.8, −0.3. Anal. Calcd for $C_{25}H_{39}NO_3SSi$: C, 65.03; H, 8.51; N, 3.03. Found: C, 65.23; H, 8.59; N, 2.99. The carbamate **25** was a colorless oil: $[\alpha]^{27}_D$ −12.1° (*c* 0.52, $CHCl_3$); MS *m/z* 462 ($M^+$ + 1, 1.2), 372 (16), 240 (12), 207 (65), 165 (18), 105 (83), 73 (20), 57 (100); IR 3450, 2170, 1725, 1675 cm$^{-1}$; $^1$H NMR $\delta$ 7.38−7.22 (m, 5H), 5.53 (d, 1H, $J$ = 6.4 Hz), 4.98 (d, 1H, $J$ = 7.3 Hz), 4.86 (quint, 1H, $J$ = 6.8 Hz), 2.81−2.65 (m, 1H), 1.83−1.20 (m, 6H), 1.49 (d, 3H, $J$ = 7.3 Hz), 1.47 (s, 9H), 0.89 (brs, 3H), 0.15 (s, 9H); $^{13}$C NMR $\delta$ 199.3, 154.1, 143.1, 128.6, 127.4, 126.0, 100.7, 92.0, 65.3, 58.3, 50.8, 48.3, 29.7, 29.2, 28.1, 22.5, 22.3, 13.8, −0.3. Anal. Calcd for $C_{25}H_{39}NO_3SSi$: C, 65.03; H, 8.51; N, 3.03. Found: C, 65.14; H, 8.58; N, 3.01.

***S-tert*-Butyl (2*R*,3*R*)- and (2*S*,3*S*)-2-Butyl-3-[[[(*R*)-1-(1-naphthyl)ethyl]amino]carboxy]-5-(trimethylsilyl)-4-pentynethioates (26 and 27).** Racemic **4b** (233 mg, 0.74 mmol) and **19** (296 mg, 1.5 mmol) afforded **26** (109 mg, 29%) and **27** (110 mg, 29%). Colorless solid **26**: mp 85.5−86.5 °C (from hexane); $[\alpha]^{20}_D$ +21.2° (*c* 0.50, $CHCl_3$); MS *m/z* 511 ($M^+$, 0.2), 240 (14), 207 (82), 182 (10), 155 (100), 127 (12), 73 (25), 57 (50); IR 3460, 2160, 1720, 1675 cm$^{-1}$; $^1$H NMR $\delta$ 8.10 (d, 1H, $J$ = 8.8 Hz), 7.86 (d, 1H, $J$ = 8.3 Hz), 7.78 (d, 1H, $J$ = 7.8 Hz), 7.57−7.40 (m, 4H), 5.65 (quint, 1H, $J$ = 6.8 Hz), 5.57 (d, 1H, $J$ = 7.3 Hz), 5.09 (d, 1H, $J$ = 7.3 Hz), 2.77 (ddd, 1H, $J$ = 3.4, 7.3, 9.8 Hz), 1.77−1.16 (m, 6H), 1.66 (d, 3H, $J$ = 6.8 Hz), 1.40 (s, 9H), 0.83 (t, 3H, $J$ = 6.8 Hz), 0.18 (s, 9H); $^{13}$C NMR $\delta$ 199.2, 154.0, 138.5, 133.9, 130.8, 128.8, 128.2, 126.4, 125.7, 125.2, 123.2, 122.1, 100.8, 92.0, 65.3, 58.5, 48.3, 46.9, 29.7, 29.1, 28.2, 22.5, 21.6, 13.8, −0.3. Anal. Calcd for $C_{29}H_{41}NO_3SSi$: C, 68.06; H, 8.08; N, 2.74. Found: C, 68.27; H, 8.25; N, 2.62. The carbamate **27** was a colorless oil: $[\alpha]^{20}_D$ −14.5° (*c* 0.50, $CHCl_3$); MS *m/z* 511 ($M^+$, 0.2), 240 (14), 207 (83), 182 (10), 155 (100), 127 (13), 73 (26), 57 (53); IR 3450, 2160, 1720, 1675 cm$^{-1}$; $^1$H NMR $\delta$ 8.12 (d, 1H, $J$ = 8.3 Hz), 7.86 (d, 1H, $J$ = 8.3 Hz), 7.78 (d, 1H, $J$ = 7.8 Hz), 7.58−7.41 (m, 4H), 5.66 (quint, 1H, $J$ = 6.8 Hz), 5.56 (d, 1H, $J$ = 6.4 Hz), 5.07 (d, 1H, $J$ = 7.3 Hz), 2.87−2.72 (m, 1H), 1.82−1.21 (m, 6H), 1.66 (d, 3H, $J$ = 6.8 Hz), 1.48 (s, 9H), 0.89 (t, 3H, $J$ = 6.8 Hz), 0.14 (s, 9H); $^{13}$C NMR $\delta$ 199.3, 154.0, 138.3, 133.9, 130.9, 128.8, 128.3, 126.4, 125.8, 125.2, 123.3, 122.3, 100.7, 92.0, 65.4, 58.3, 48.3, 46.8, 29.7, 29.2, 28.1, 22.5, 21.5, 13.8, −0.3. Anal. Calcd for

$C_{29}H_{41}NO_3SSi$: C, 68.06; H, 8.08; N, 2.74. Found: C, 68.14; H, 8.17; N, 2.61.

***S*-*tert*-Butyl (2*R*,3*S*)- and (2*S*,3*R*)-2-Ethyl-3-[[[(*S*)-1-phenylethyl]amino]carboxy]-5-(trimethylsilyl)-4-pentynethioates (28 and 29).** Racemic aldol **5a** (250 mg, 0.87 mmol) and **18** (258 mg, 1.8 mmol) produced **28** (159 mg, 42%) and **29** (150 mg, 40%). Colorless solid **28**: mp 136.5–137.0 °C (from hexane); $[\alpha]^{23}_D$ −96.9° (*c* 0.50, $CHCl_3$); MS *m/z* 434 ($M^+$ + 1, 0.1), 344 (29), 179 (88), 137 (30), 105 (100), 57 (55); IR 3450, 2170, 1725, 1675 cm$^{-1}$; $^1$H NMR δ 7.36–7.21 (m, 5H), 5.49 (d, 1H, *J* = 8.8 Hz), 4.99 (d, 1H, *J* = 5.9 Hz), 4.85 (m, 1H), 2.73 (ddd, 1H, *J* = 5.4, 8.8, 8.8 Hz), 1.78–1.66 (m, 2H), 1.48 (d, 3H, *J* = 6.4 Hz), 1.38 (s, 9H), 0.95 (t, 3H, *J* = 6.8 Hz), 0.17 (s, 9H); $^{13}$C NMR δ 199.6, 153.9, 143.3, 128.5, 127.3, 125.9, 101.1, 92.1, 65.5, 59.6, 50.6, 48.4, 29.6, 22.6, 22.3, 11.3, −0.3. Anal. Calcd for $C_{23}H_{35}NO_3SSi$: C, 63.70; H, 8.13; N, 3.23. Found: C, 63.56; H, 8.09; N, 3.15. Colorless solid **29**: mp 117.0–117.5 °C (from hexane); $[\alpha]^{23}_D$ +56.8° (*c* 0.50, $CHCl_3$); MS *m/z* 434 ($M^+$ + 1, 3.5), 344 (22), 179 (47), 137 (28), 105 (100), 57 (84); IR 3450, 2160, 1725, 1680 cm$^{-1}$; $^1$H NMR δ 7.36–7.23 (m, 5H), 5.51 (d, 1H, *J* = 9.3 Hz), 4.98 (d, 1H, *J* = 6.8 Hz), 4.85 (dq, 1H, *J* = 6.8, 6.8 Hz), 2.80–2.67 (m, 1H), 1.81–1.63 (m, 2H), 1.47 (s, 9H), 1.46 (d, 3H, *J* = 6.8 Hz), 0.97 (t, 3H, *J* = 6.8 Hz), 0.14 (s, 9H); $^{13}$C NMR δ 199.7, 153.9, 143.1, 128.6, 127.4, 126.0, 101.0, 92.2, 65.5, 59.6, 50.6, 48.4, 29.7, 22.5, 22.2, 11.3, −0.3. Anal. Calcd for $C_{23}H_{35}NO_3SSi$: C, 63.70; H, 8.13; N, 3.23. Found: C, 63.79; H, 8.02; N, 3.13.

***S*-*tert*-Butyl (2*R*,3*S*)- and (2*S*,3*R*)-2-Ethyl-3-[[[(*R*)-1-(1-naphtyl)ethyl]amino]carboxy]-5-(trimethylsilyl)-4-pentynethioates (30 and 31).** Treatment of **5a** (206 mg, 0.72 mmol) and **19** (298 mg, 1.5 mmol) furnished **30** (122 mg, 35%) and **31** (120 mg, 35%). Colorless solid **30**: mp 103.0–103.5 °C (from ether): $[\alpha]^{25}_D$ +55.5° (*c* 0.50, $CHCl_3$); MS *m/z* 483 ($M^+$, 0.4), 200 (8.5), 179 (16), 155 (100), 137 (21), 127 (20), 73 (13), 57 (96); IR 3450, 2160, 1725, 1675 cm$^{-1}$; $^1$H NMR δ 8.10 (d, 1H, *J* = 8.3 Hz), 7.84 (d, 1H, *J* = 7.8 Hz), 7.70 (d, 1H, *J* = 7.8 Hz), 7.57–7.36 (m, 4H), 5.65 (dq, 1H, *J* = 6.8, 6.8 Hz), 5.52 (d, 1H, *J* = 9.3 Hz), 5.09 (d, 1H, *J* = 6.8 Hz), 2.72 (ddd, 1H, *J* = 4.9, 9.3, 9.3 Hz), 1.75–1.59 (m, 2H), 1.65 (d, 3H, *J* = 6.8 Hz), 1.29 (s, 9H), 0.94 (t, 3H, *J* = 7.3 Hz), 0.18 (s, 9H); $^{13}$C NMR δ 199.6, 153.9, 138.7, 133.9, 130.8, 128.7, 128.2, 126.4, 125.7, 125.2, 123.2, 122.1, 101.1, 92.2, 65.6, 59.5, 48.4, 46.8, 29.5, 22.5, 21.7, 11.3, −0.3. Anal. Calcd for $C_{27}H_{37}NO_3SSi$: C, 67.04; H, 7.71; N, 2.90. Found: C, 67.03; H, 7.75; N, 2.88. Colorless solid **31**: mp 113.5–114.0 °C (from ether): $[\alpha]^{25}_D$ −83.4° (*c* 0.50, $CHCl_3$); MS *m/z* 483 ($M^+$, 0.3), 214 (12), 200 (13), 179 (29), 155 (100), 137 (17), 127 (15), 57 (77); IR 3450, 2160, 1725, 1675 cm$^{-1}$; $^1$H NMR δ 8.12 (d, 1H, *J* = 8.3 Hz), 7.86 (dd, 1H, *J* = 1.5, 7.3 Hz), 7.78 (d, 1H, *J* = 7.8 Hz), 7.57–7.40 (m, 4H), 5.65 (quint, 1H, *J* = 6.8 Hz), 5.54 (d, 1H, *J* = 9.3 Hz), 5.05 (d, 1H, *J* = 7.3 Hz), 2.79–2.67 (m, 1H), 1.78–1.67 (m, 2H), 1.63 (d, 3H, *J* = 6.8 Hz), 1.48 (s, 9H), 0.97 (t, 3H, *J* = 6.8 Hz), 0.13 (s, 9H); $^{13}$C NMR δ 199.8, 153.9, 138.4, 133.9, 130.9, 128.8, 128.3, 126.4, 125.7, 125.2, 123.3, 122.2, 101.0, 92.1, 65.6, 59.6, 48.4, 46.7, 29.7, 22.6, 21.5, 11.3, −0.3. Anal. Calcd for $C_{27}H_{37}NO_3SSi$: C, 66.75; H, 7.71; N, 2.79. Found: C, 67.10; H, 7.75; N, 2.83.

**General Procedure for Removal of Chiral Auxiliary.** To a solution of carbamate (0.25 mmol) and triethylamine (0.16 mL, 1.1 mmol) in dry benzene (3.0 mL) was added trichlorosilane (0.1 mL, 1.0 mmol) under nitrogen atmosphere at rt. After being stirred overnight, the reaction mixture was quenched by addition of saturated ammonium chloride solution (0.1 mL) and stirred for 10 min. The white precipitates were filtered off by suction, and the filtrate was dried and concentrated. Chromatography of the residue with hexane–ethyl acetate (30:1) afforded the chiral aldol.

***S*-*tert*-Butyl (2*R*,3*R*)- and (2*S*,3*S*)-2-Ethyl-3-hydroxy-5-(trimethylsilyl)-4-pentynethioates (4a) from 20 and 21.** Treatment of **20** (130 mg, 0.30 mmol) with trichlorosilane (0.1 mL, 1.0 mmol) under the conditions described in the general procedure gave (+)-**4a** (64 mg, 75%) as a colorless oil: $[\alpha]^{22}_D$ +44.8° (*c* 0.51, $CHCl_3$). Anal. Calcd for $C_{14}H_{26}O_2SSi$: C, 58.69; H, 9.15. Found: C, 58.76; H, 9.21. Similar treatment of **21** (130 mg, 0.30 mmol) with trichlorosilane (0.1 mL, 1.0 mmol) yielded (−)-**4a** (72 mg, 84%) as a colorless oil: $[\alpha]^{22}_D$ −44.2° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{14}H_{26}O_2SSi$: C, 58.69; H, 9.15. Found: C, 58.69; H, 9.19.

***S*-*tert*-Butyl (2*R*,3*R*)- and (2*S*,3*S*)-2-Ethyl-3-hydroxy-5-(trimethylsilyl)-4-pentynethioates (4a) from 22 and 23.** The chiral (−)-**4a** (38 mg, 86%) was obtained from **22** (75 mg, 0.16 mmol) and trichlorosilane (0.1 mL, 1.0 mmol). The chiral (−)-**4a** was a colorless oil: $[\alpha]^{22}_D$ −44.1° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{14}H_{26}O_2SSi$: C, 58.69; H, 9.15. Found: C, 58.51; H, 9.06. Reaction of **23** (70 mg, 0.14 mmol) with trichlorosilane (0.1 mL, 1.0 mmol) produced (+)-**4a** (36 mg, 87%) as a colorless oil: $[\alpha]^{22}_D$ +44.3° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{14}H_{26}O_2SSi$: C, 58.69; H, 9.15. Found: C, 58.64; H, 9.16.

***S*-*tert*-Butyl (2*R*,3*R*)- and (2*S*,3*S*)-2-Butyl-3-hydroxy-5-(trimethylsilyl)-4-pentynethioates (4b) from 24 and 25.** Treatment of **24** (110 mg, 0.24 mmol) with trichlorosilane (0.1 mL, 1.0 mmol) afforded (+)-**4b** (53 mg, 71%) as a colorless oil: $[\alpha]^{27}_D$ +29.5° (*c* 0.51, $CHCl_3$). Anal. Calcd for $C_{16}H_{30}O_2SSi$: C, 61.09; H, 9.61. Found: C, 61.01; H, 9.62. The carbamate **25** (110 mg, 0.24 mmol) and trichlorosilane (0.1 mL, 1.0 mmol) gave (−)-**4b** (63 mg, 84%) as a colorless oil: $[\alpha]^{27}_D$ −26.1° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{16}H_{30}O_2SSi$: C, 61.09; H, 9.61. Found: C, 60.98; H, 9.63.

***S*-*tert*-Butyl (2*R*,3*R*)- and (2*S*,3*S*)-2-Butyl-3-hydroxy-5-(trimethylsilyl)-4-pentynethioates (4b) from 26 and 27.** Reaction of **26** (85 mg, 0.17 mmol) with trichlorosilane (0.1 mL, 1.0 mmol) provided (−)-**4b** (41 mg, 78%) as a colorless oil: $[\alpha]^{27}_D$ −26.8° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{16}H_{30}O_2SSi$: C, 61.09; H, 9.61. Found: C, 61.06; H, 9.64. Treatment of **27** (100 mg, 0.20 mmol) with trichlorosilane (0.1 mL, 1.0 mmol) yielded (+)-**4b** (51 mg, 83%) as a colorless oil: $[\alpha]^{27}_D$ +27.4° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{16}H_{30}O_2SSi$: C, 61.09; H, 9.61. Found: C, 61.00; H, 9.67.

***S*-*tert*-Butyl (2*R*,3*S*)- and (2*S*,3*R*)-2-Ethyl-3-hydroxy-5-(trimethylsilyl)-4-pentynethioate (5a) from 28 and 29.** The aldol (−)-**5a** (82 mg, 83%) was provided by treatment of carbamate **28** (150 mg, 0.35 mmol) with trichlorosilane (0.1 mL, 1.0 mmol) as a colorless solid: mp 40–41 °C (from hexane); $[\alpha]^{22}_D$ −75.8° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{14}H_{26}O_2SSi$: C, 58.69; H, 9.15. Found: C, 58.62; H, 9.15. The carbonate **29** (150 mg, 0.35 mmol) and trichlorosilane (0.1 mL, 1.0 mmol) yielded (+)-**5a** (79 mg, 80%) as a colorless solid: mp 40–41 °C (from hexane); $[\alpha]^{22}_D$ +77.5° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{14}H_{26}O_2SSi$: C, 58.69; H, 9.15. Found: C, 58.59; H, 9.13.

***S*-*tert*-Butyl (2*R*,3*S*)- and (2*S*,3*R*)-2-Ethyl-3-hydroxy-5-(trimethylsilyl)-4-pentynethioate (5a) from 30 and 31.** The carbamate **30** (100 mg, 0.21 mmol) and trichlorosilane (0.1 mL, 1.0 mmol) afforded (−)-**5a** (49 mg, 83%) as a colorless solid: mp 40–41 °C (from hexane); $[\alpha]^{22}_D$ −76.3° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{14}H_{26}O_2SSi$: C, 58.69; H, 9.15. Found: C, 58.46; H, 9.19. Treatment of **31** (95 mg, 0.20 mmol) with trichlorosilane (0.1 mL, 1.0 mmol) furnished (+)-**5a** (46 mg, 82%) as a colorless solid: mp 40–41 °C (from hexane); $[\alpha]^{22}_D$ +74.9° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{14}H_{26}O_2SSi$: C, 58.69; H, 9.15. Found: C, 58.79; H, 9.24.

**Hexacarbonyl-*μ*-($\eta^4$-4-methyl-2-pentynal)dicobalt (Co–Co) (16).** To a solution of propynyl alcohol **32** (490 mg, 5.0 mmol)[16] in dry $CH_2Cl_2$ (10 mL) was added PCC (1.7 g, 7.9 mmol) portionwise at rt. After being stirred for 6 h, the reaction mixture was diluted with ether and passed through a short pad of Florisil to give the crude aldehyde. $Co_2(CO)_8$ (2.0 g, 5.8 mmol) was added to the ethereal solution of the crude aldehyde at rt, and the mixture was stirred for 1 h. After removal of volatile materials, the residue was purified by column chromatography (hexane–$CH_2Cl_2$ = 10:1 → 3:1) to give the cobalt complex **16** (1.1 g, 58%): MS *m/z* 382 ($M^+$, 1.5), 354 (16), 326 (22), 298 (24), 270 (35), 242 (30), 214 (33), 118 (25), 28 (100); IR 2080, 2040, 2010, 1665 cm$^{-1}$; $^1$H NMR δ 10.34 (s, 1H), 3.12 (hept, *J* = 6.9 Hz), 1.32 (d, 6H, *J* = 6.9 Hz); $^{13}$C NMR δ 198.2, 190.9, 109.6, 87.1, 32.9, 29.7, 24.7. Anal. Calcd for $C_{12}H_8Co_2O_7$: C, 37.73; H, 2.11. Found: C, 37.77; H, 2.29.

***S*-*tert*-Butyl (2*R**,3*S**)- and (2*R**,3*R**)-2-(Benzyloxy)-3-hydroxy-6-methyl-4-heptynethioates (15 and 34).** To a solution of aldehyde **16** (20.0 mg, 0.05 mmol) in dry $CH_2Cl_2$ (1.0 mL) was added dropwise a solution of $BF_3{\cdot}OEt_2$ in dry $CH_2Cl_2$ (1.0 M solution; 0.5 mL, 0.5 mmol) at −78 °C. After the mixture was stirred for 30 min, a solution of acetal **20** (160 mg, 0.5 mmol) in dry $CH_2Cl_2$ (0.5 mL) was added to the reaction mixture. The reaction mixture was kept at the same temperature for 30 min until the starting aldehyde **16** was consumed (monitored by TLC). Reaction was quenched by addition of saturated ammonium chloride solution (1.0 mL). The reaction mixture was washed with water and brine, dried, and concentrated. CAN (120 mg, 0.2 mmol) was added portionwise to a solution of the crude aldol products with cobalt complexation in methanol (3.0 mL) at 0 °C. The reaction mixture was stirred for 30 min (monitored by TLC), and the methanol was evaporated off. The residue was diluted with water and extracted three times with ethyl acetate. The combined ethyl acetate layers were washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–ethyl acetate (30:1) gave aldol products **15** and **34** (15.5 mg, 89%, **15**:**34** = 95:5). The diastereomers **15** and **34** could be easily purified by column chromatography. The *syn*-aldol **15** was a colorless solid: mp 38.0–38.5 °C (from hexane); MS *m/z* 335 (M$^+$ + 1, 0.3), 238 (91), 182 (66), 147 (19), 121 (16), 92 (100), 57 (99); IR 3575, 2225, 1675 cm$^{-1}$; $^1$H NMR δ 7.46–7.29 (m, 5H), 4.85 and 4.66 (ABq, *J* = 11 Hz), 4.60 (ddd, 1H, *J* = 2.0, 4.4, 7.8 Hz), 3.89 (d, 1H, *J* = 4.4 Hz), 2.69 (d, 1H, *J* = 7.8 Hz), 2.57 (dhept, *J* = 2.0, 6.8 Hz), 1.48 (s, 9H), 1.15 (d, 6H, *J* = 6.8 Hz); $^{13}$C NMR δ 200.6, 136.7, 128.4, 128.2, 128.2, 92.7, 87.1, 76.4, 74.2, 63.6, 47.6, 29.7, 22.7, 20.5. Anal. Calcd for $C_{19}H_{26}O_3S$: C, 68.23; H, 7.84. Found: C, 68.23; H, 7.84. The *anti*-compound **34** was a colorless oil: MS *m/z* 335 (M$^+$ + 1, 4.4), 238 (62), 182 (46), 147 (10), 121 (7.1), 91 (100), 57 (51); IR 3575, 2225, 1670 cm$^{-1}$; $^1$H NMR δ 7.45–7.29 (m, 5H), 4.89 and 4.59 (ABq, *J* = 12 Hz), 4.63 (ddd, 1H, *J* = 2.0, 4.9, 8.3 Hz), 3.95 (d, 1H, *J* = 4.9 Hz), 2.60 (d, 1H, *J* = 8.3 Hz), 2.58 (dhept, *J* = 2.0, 6.8 Hz), 1.49 (s, 9H), 1.15 (d, 6H, *J* = 6.8 Hz); $^{13}$C NMR δ 200.6, 136.9, 128.4, 128.1, 128.1, 92.9, 86.6, 75.9, 74.1, 63.7, 47.6, 29.7, 22.7, 20.5. Anal. Calcd for $C_{19}H_{26}O_3S$: C, 68.23; H, 7.84. Found: C, 68.00; H, 7.83.

***S*-*tert*-Butyl (2*S*,3*R*)- and (2*R*,3*S*)-2-(Benzyloxy)-3-[[[(*S*)-1-phenylethyl]amino]carboxy]-6-methyl-4-heptynethioates (35 and 36).** According to the general procedure for optical resolution, **35** (149 mg, 35%) and **36** (150 mg, 35%) were obtained by treatment of (±)-**15** (296 mg, 0.88 mmol) with (*S*)-1-phenylethyl isocyanate **18** (260 mg). The carbamate **35** was a colorless oil: $[\alpha]^{27}_{D}$ +58.2° (*c* 0.50, $CHCl_3$); MS *m/z* 482 (M$^+$ + 1, 0.2), 364 (29), 238 (18), 210 (15), 182 (13), 105 (99), 91 (100), 57 (51); IR 3450, 2225, 1725, 1675 cm$^{-1}$; $^1$H NMR δ 7.42–7.19 (m, 10H), 5.70 (brs, 1H), 5.10 (d, 1H, *J* = 7.3 Hz), 4.88–4.76 (m, 1H), 4.83 and 4.62 (ABq, 2H, *J* = 12 Hz), 3.95 (d, 1H, *J* = 3.7 Hz), 2.64–2.47 (m, 1H), 1.46 (d, 3H, *J* = 7.3 Hz), 1.39 (s, 9H), 1.15 (d, 6H, *J* = 6.4 Hz); $^{13}$C NMR δ 199.0, 153.9, 143.3, 136.8, 128.5, 128.3, 128.2, 127.9, 127.2, 125.9, 93.4, 85.9, 74.0, 73.2, 64.8, 50.7, 47.4, 29.6, 22.5, 22.4, 20.5. Anal. Calcd for $C_{28}H_{35}NO_4S$: C, 69.82; H, 7.32; N, 2.90. Found: C, 69.75; H, 7.48; N, 2.82. The carbamate **36** was a colorless oil: $[\alpha]^{27}_{D}$ −111° (*c* 0.50, $CHCl_3$); MS *m/z* 482 (M$^+$ + 1, 5.1), 364 (61), 238 (26), 210 (22), 182 (17), 154 (12), 105 (93), 91 (100); IR 3450, 2225, 1725, 1675 cm$^{-1}$; $^1$H NMR δ 7.47–7.19 (m, 10H), 5.72 (brs, 1H), 5.11 (d, 1H, *J* = 7.3 Hz), 4.90–4.76 (m, 1H), 4.85 and 4.64 (ABq, 2H, *J* = 12 Hz), 3.98 (d, 1H, *J* = 4.7 Hz), 2.61–2.46 (m, 1H), 1.48 (s, 9H), 1.43 (d, 3H, *J* = 7.3 Hz), 1.15 (d, 6H, *J* = 6.4 Hz); $^{13}$C NMR δ 199.0, 154.0, 143.1, 136.8, 128.5, 128.3, 128.2, 127.9, 127.2, 125.9, 93.5, 85.9, 74.0, 73.6, 64.8, 50.7, 47.4, 29.6, 22.4, 22.3, 20.4. Anal. Calcd for $C_{28}H_{35}NO_4S$: C, 69.82; H, 7.32; N, 2.90. Found: C, 69.58; H, 7.45; N, 2.86.

***S*-*tert*-Butyl (2*R*,3*S*)- and (2*S*,3*R*)-2-(Benzyloxy)-3-[[[(*R*)-1-(1-naphthyl)ethyl]amino]carboxy]-6-methyl-4-heptynethioates (37 and 38).** Similar treatment of (±)-**15** (200 mg, 0.60 mmol) with (*R*)-1-(1-naphthyl)ethyl isocyanate **19** (245 mg, 1.2 mmol) afforded **37** (102 mg, 32%) and **38** (102 mg, 32%). The carbamate **37** was a colorless oil: $[\alpha]^{20}_{D}$ +77.4° (*c* 0.50, $CHCl_3$); MS *m/z* 531 (M$^+$, 0.07), 414 (11), 245 (15), 215 (14), 182 (21), 155 (97), 127 (11), 91 (100), 57 (36); IR 3450, 2225, 1725, 1675 cm$^{-1}$; $^1$H NMR δ 8.09 (d, 1H, *J* = 8.3 Hz), 7.84 (dd, 1H, *J* = 2.0, 7.3 Hz), 7.76 (d, 1H, *J* = 7.8 Hz), 7.52–7.16 (m, 9H), 5.71 (brd, 1H, *J* = 2.9 Hz), 5.64 (quint, 1H, *J* = 6.8 Hz), 5.15 (d, 1H, *J* = 7.3 Hz), 4.79 and 4.58 (ABq, 2H, *J* = 12 Hz), 3.93 (d, 1H, *J* = 4.4 Hz), 2.64–2.51 (m, 1H), 1.63 (d, 3H, *J* = 6.8 Hz), 1.34 (s, 9H), 1.16 (d, 6H, *J* = 6.8 Hz); $^{13}$C NMR δ 198.9, 153.9, 138.7, 136.7, 133.9, 130.7, 128.7, 128.2, 128.1, 127.9, 126.4, 125.7, 125.2, 123.2, 122.1, 93.5, 85.9, 74.0, 73.7, 65.0, 47.5, 46.9, 29.6, 22.5, 21.8, 20.53. Anal. Calcd for $C_{32}H_{37}NO_4S$: C, 72.29; H, 7.01; N, 2.63. Found: C, 71.99; H, 7.16; N, 2.63. The carbamate **38** was a colorless oil: $[\alpha]^{20}_{D}$ −68.6° (*c* 0.50, $CHCl_3$); MS *m/z* 532 (M$^+$ + 1, 0.09), 414 (21), 245 (23), 215 (19), 182 (24), 155 (100), 127 (16), 91 (99), 57 (52); IR 3450, 2225, 1725, 1675 cm$^{-1}$; $^1$H NMR δ 8.12 (d, 1H, *J* = 8.8 Hz), 7.85 (d, 1H, *J* = 7.6 Hz), 7.77 (d, 1H, *J* = 7.8 Hz), 7.57–7.25 (m, 9H), 5.71 (brd, 1H, *J* = 2.4 Hz), 5.64 (quint, 1H, *J* = 6.8 Hz), 5.16 (d, 1H, *J* = 6.8 Hz), 4.85 and 4.64 (ABq, 2H, *J* = 11 Hz), 3.99 (d, 1H, *J* = 4.4 Hz), 2.59–2.47 (m, 1H), 1.60 (d, 3H, *J* = 6.8 Hz), 1.50 (s, 9H), 1.11 (d, 3H, *J* = 6.8 Hz), 1.10 (d, 3H, *J* = 7.4 Hz); $^{13}$C NMR δ 199.1, 154.0, 138.6, 136.8, 133.9, 130.8, 128.8, 128.3, 128.2, 128.2, 128.0, 126.3, 125.7, 125.2, 123.3, 122.2, 93.6, 86.0, 74.0, 73.6, 65.0, 47.5, 46.8, 29.7, 22.6, 22.5, 21.7, 20.5. Anal. Calcd for $C_{32}H_{37}NO_4S$: C, 72.29; H, 7.01; N, 2.63. Found: C, 72.34; H, 7.08; N, 2.60.

***S*-*tert*-Butyl (2*S*,3*R*)-2-(Benzyloxy)-3-hydroxy-6-methyl-4-heptynethioate [(−)-15].** According to the general procedure for removal of chiral auxiliary, treatment of **35** (149 mg, 0.31 mmol) with trichlorosilane (0.1 mL, 1.0 mmol) yielded (−)-**15** (89 mg, 86%) as a colorless solid: mp 38.0–39.0 °C (from hexane); $[\alpha]^{24}_{D}$ −87.1° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{19}H_{26}O_3S$: C, 68.23; H, 7.84. Found: C, 68.15; H, 7.83.

***S*-*tert*-Butyl (2*R*,3*S*)-2-(Benzyloxy)-3-hydroxy-6-methyl-4-heptynethioate [(+)-15].** Similar treatment of **36** (150 mg, 0.31 mmol) with trichlorosilane (0.1 mL, 1.0 mmol) afforded (+)-**15** (88 mg, 84%) as a colorless solid: mp 38.0–38.5 °C (from hexane); $[\alpha]^{24}_{D}$ +86.8° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{19}H_{26}O_3S$: C, 68.23; H, 7.84. Found: C, 68.44; H, 7.85.

***S*-*tert*-Butyl (2*R*,3*S*)-2-(Benzyloxy)-3-hydroxy-6-methyl-4-heptynethioate [(+)-15].** The carbamate **37** (102 mg, 0.19 mmol) and trichlorosilane (0.1 mL, 1.0 mmol) furnished (+)-**15** (47 mg, 73%) as a colorless solid: mp 38.0–39.0 °C (from hexane); $[\alpha]^{23}_{D}$ +86.6° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{19}H_{26}O_3S$: C, 68.23; H, 7.84. Found: C, 67.99; H, 8.06.

***S*-*tert*-Butyl (2*S*,3*R*)-2-(Benzyloxy)-3-hydroxy-6-methyl-4-heptynethioate [(−)-15].** The chiral aldol (−)-**15** (49 mg, 76%) was obtained by treatment of **38** (102 mg, 0.19 mmol) with trichlorosilane (0.1 mL, 1.0 mmol). Colorless solid product (−)-**15**: mp 37.5–38.0 °C (from hexane); $[\alpha]^{23}_{D}$ −86.7° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{19}H_{26}O_3S$: C, 68.23; H, 7.84. Found: C, 68.20; H, 7.81.

**(2*R*,3*R*)-2-(Benzyloxy)-6-methyl-4-heptene-1,3-diol [(−)-39].** To a solution of (−)-**15** (100 mg, 0.30 mmol) in ether (10 mL) was added LAH (60 mg, 1.58 mmol) at 0 °C. The reaction mixture was refluxed for 3 h. Excess LAH was decomposed by addition of water. The resulting mixture was passed through a short pad of Celite and concentrated *in vacuo*. The residue was purified by column chromatography with hexane–ethyl acetate (3:1) to afford diol (−)-**39** (57 mg, 76%) as a colorless solid: mp 39–40 °C (from hexane); $[\alpha]^{23}_{D}$ −14.5° (*c* 0.50, $CHCl_3$); MS *m/z* 250 (M$^+$, 0.5), 189 (24), 134 (34), 126 (18), 99 (64), 91 (100), 81 (22), 65 (17); IR 3570 cm$^{-1}$; $^1$H NMR δ 7.44–7.24 (m, 5H), 5.78 (dd, 1H, *J* = 6.3, 16 Hz), 5.44 (ddd, 1H, *J* = 1.0, 6.9, 16 Hz), 4.73 and 4.67 (ABq, 1H, *J* = 12 Hz), 4.20 (t, 1H, *J* = 6.3 Hz), 3.80 (dd, 1H, *J* = 4.3, 12 Hz), 3.65 (dd, 1H, *J* = 4.3, 12 Hz), 3.43 (ddd, 1H, *J* = 4.3, 4.3, 6.3 Hz), 2.42–2.21 (m, 1H), 1.66 (brs, 2H), 1.00 (d, 6H, *J* = 6.9 Hz); $^{13}$C NMR δ 141.6, 137.9, 128.6, 128.1, 128.0, 125.6, 82.3, 73.1, 73.1, 61.5, 30.8, 22.2, 22.1. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.80; H, 9.05.

**(2*S*,3*S*)-2-(Benzyloxy)-6-methyl-4-heptene-1,3-diol [(+)-39].** Similar treatment of (+)-**15** (100 mg, 0.30 mmol) with LAH (54 mg, 1.42 mmol) afforded (+)-**39** (42 mg, 56%) as a colorless solid: mp 39–40 °C (from hexane); $[\alpha]^{23}_{D}$ +14.8° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.67; H, 9.10.

**(2*R*,3*R*)-2,3-Bis(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-6-methyl-4-heptene [(−)-40].** To a solution of (−)-**39** (105 mg, 0.42 mmol), triethylamine (0.15 mL, 1.1 mmol), and DMAP (2.4 mg, 0.02 mmol) in $CH_2Cl_2$ (2.0 mL) was added a solution of TBDMSCl (76 mg, 0.50 mmol) in $CH_2Cl_2$ (1.0 mL) at rt. After being stirred overnight, the reaction mixture was diluted with water and extracted with $CH_2Cl_2$. The extract was washed successively with water and brine, dried, and concentrated to dryness to give the crude monosilylated compound. Sodium hydride (60% oil dispersion; 50 mg, 1.3 mmol) was added to a solution of the crude monosilylated compound in THF (3.0 mL) at 0 °C, and the reaction mixture was stirred for 1 h at the same temperature. Tetrabutylammonium iodide (10 mg, 0.03 mmol) and benzyl bromide (0.10 mL, 0.84 mmol) was added successively to the reaction mixture and stirring was continued overnight at rt. Reaction mixture was quenched by addition of water and extracted with ethyl acetate. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane−$CH_2Cl_2$ (5:1 → 2:1) to give (−)-**40** (168 mg, 88%) as a colorless oil: $[\alpha]^{18}{}_D$ −25.3° (*c* 0.53, $CHCl_3$); IR 2950 $cm^{-1}$; $^1H$ NMR $\delta$ 7.43−7.19 (m, 10H), 5.63 (dd, 1H, *J* = 6.3, 16 Hz), 5.41 (ddd, 1H, *J* = 1.0, 8.3, 16 Hz), 4.74 and 4.69 (ABq, 1H, *J* = 12 Hz), 4.59 and 4.37 (ABq, 1H, *J* = 12 Hz), 3.87 (dd, 1H, *J* = 5.0, 7.9 Hz), 3.77 (dd, 1H, *J* = 4.3, 11 Hz), 3.66 (dd, 1H, *J* = 6.3, 11 Hz), 3.49 (dt, 1H, *J* = 6.3, 5.0 Hz), 2.42−2.21 (m, 1H), 1.01 (d, 3H, *J* = 6.6 Hz), 0.99 (d, 3H, *J* = 6.9 Hz), 0.88 (s, 9H), 0.02 (s, 6H); $^{13}C$ NMR $\delta$ 142.2, 139.1, 138.8, 128.2, 128.1, 128.0, 127.8, 127.3, 127.3, 124.1, 82.7, 80.1, 73.6, 70.2, 63.4, 30.9, 25.9, 22.3, 22.3, 18.3, −5.3, −5.4. Anal. Calcd for $C_{28}H_{42}O_3Si$: C, 73.96; H, 9.31. Found: C, 74.36; H, 9.37.

**(2*S*,3*S*)-2,3-Bis(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-6-methyl-4-heptene [(+)-40].** Similar treatment of (+)-**39** (102 mg, 0.41 mmol) with TBDMSCl (78 mg, 0.52 mmol) in the presence of triethylamine (0.12 mL, 0.86 mmol) and DMAP (2.2 mg, 0.02 mmol) provided the monosilylated compound, which was reacted with sodium hydride (60% oil dispersion; 50 mg, 1.3 mmol), tetrabutylammonium iodide (10 mg, 0.03 mmol), and benzyl bromide (0.10 mL, 0.84 mmol) to give (+)-**40** (155 mg, 83%). The compound (+)-**40** was a colorless oil: $[\alpha]^{23}{}_D$ +26.5° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{28}H_{42}O_3Si$: C, 73.96; H, 9.31. Found: C, 74.08; H, 9.29.

**2,3-Di-*O*-benzyl-4-*O*-(*tert*-butyldimethylsilyl)-D-threitol [(−)-41].** Ozone was bubbled through a solution of (−)-**40** (100 mg, 0.22 mmol) in methanol (3.0 mL) at −78 °C for 1 min. The ozone flow was replaced by nitrogen. After the excess ozone was removed, the reaction mixture was allowed to warm up to rt. Sodium borohydride (100 mg, 2.6 mmol) was added to the reaction mixture. After the mixture was stirred for 1 h, the methanol was evaporated off to leave the residue, which was diluted with water and extracted with ethyl acetate. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−ethyl acetate (3:1) provided (−)-**41** (49 mg, 53%) as a colorless oil: $[\alpha]^{22}{}_D$ −14.4° (*c* 0.50, $CHCl_3$); Ms *m/z* 417 ($M^+$ + 1, 8.3), 219 (10), 181 (51), 117 (13), 91 (100), 65 (14); IR 3440 $cm^{-1}$; $^1H$ NMR $\delta$ 7.39−7.23 (m, 5H), 4.72 and 4.62 (ABq, 2H, *J* = 12 Hz), 4.66 and 4.62 (ABq, 2H *J* = 12 Hz), 3.84−3.60 (m, 6H), 2.21 (brs, 1H), 0.90 (s, 9H), 0.06 (s, 6H); $^{13}C$ NMR $\delta$ 138.3, 138.4, 128.4, 128.4, 128.0, 127.9, 127.7, 127.7, 80.2, 79.3, 73.0, 72.8, 62.3, 61.5, 25.8, 18.2, −5.5. Anal. Calcd for $C_{24}H_{36}O_4Si$: C, 69.19; H, 8.71. Found: C, 69.42; H, 8.81.

**2,3-Di-*O*-benzyl-4-*O*-(*tert*-butyldimethylsilyl)-L-threitol [(+)-41].** Similar treatment of (+)-**40** (109 mg, 0.24 mmol) with ozone and sodium borohydride (100 mg, 2.6 mmol) provided (+)-**41** (41 mg, 41%) as a colorless oil: $[\alpha]^{22}{}_D$ +13.9° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{24}H_{36}O_4Si$: C, 69.19; H, 8.71. Found: C, 69.25; H, 8.80. An authentic sample was obtained as follows: Sodium hydride (60% oil dispersion: 16 mg, 0.40 mmol) was added to a solution of 2,3-di-*O*-benzyl-L-threitol (**42**)[21] (110 mg, 0.36 mmol) in THF (4.0 mL) at rt, and the reaction mixture was stirred for 1 h. A solution of TBDMSCl (60 mg, 0.40 mmol) in THF (1.0 mL) was added to the reaction mixture, and vigorous stirring was continued for an additional hour. The reaction mixture was diluted with water and extracted with ethyl acetate. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−ethyl acetate (3:1) provided **44** (118 mg, 78%) as a colorless oil: $[\alpha]^{17}{}_D$ +13.3° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{24}H_{36}O_4Si$: C, 69.19; H, 8.71. Found: C, 69.34; H, 8.81.

***S*-*tert*-Butyl (2*S*,3*R*)-2-(Benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-methyl-4-heptynethioate (43).** To a solution of (−)-**15** (290 mg, 0.87 mmol) and imidazole (90 mg, 1.3 mmol) in DMF (0.02 mL) was added a solution of TBDMSCl (390 mg, 2.6 mmol) in DMF (0.03 mL) at rt. After being stirred for 30 min, the reaction mixture was diluted with water and extracted with ether. The extracts were washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−$CH_2Cl_2$ (2:1) afforded the silyl ether **43** (370 mg, 95%) as a colorless oil: $[\alpha]^{27}{}_D$ −95.8° (*c* 0.50, $CHCl_3$); MS *m/z* 449 ($M^+$ + 1, 3.8), 391 (21), 335 (31), 211 (100), 183 (82), 91 (99), 73 (46), 57 (66); IR 2230, 1675 $cm^{-1}$; $^1H$ NMR $\delta$ 7.43−7.25 (m, 5H), 4.80 and 4.65 (ABq, 2H, *J* = 12 Hz), 4.66 (dd, 1H, *J* = 2.4, 5.4 Hz), 3.81 (d, 1H, *J* = 5.4 Hz), 2.53 (dhept, 1H, *J* = 2.4, 6.8 Hz), 1.47 (s, 9H), 1.13 (d, 3H, *J* = 6.8 Hz), 1.12 (d, 3H, *J* = 6.8 Hz), 0.90 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H); $^{13}C$ NMR $\delta$ 199.9, 137.4, 128.2, 128.1, 127.7, 92.7, 88.8, 77.3, 73.7, 64.7, 47.3, 29.8, 25.8, 22.6, 20.5, 18.3, −4.6, −4.8. Anal. Calcd for $C_{25}H_{40}O_3SSi$: C, 66.91; H, 8.99. Found: C, 67.15; H, 9.05.

***S*-*tert*-Butyl (2*R*,3*S*,4*R*,5*R*)-4-(Benzyloxy)-5-[(*tert*-butyldimethylsilyl)oxy]-3-hydroxy-2-methoxy-8-methyl-6-nonynethioate (45).** To a solution of **43** (300 mg, 0.67 mmol) in dry $CH_2Cl_2$ (7.0 mL) at −78 °C was added dropwise DIBALH (1 M toluene solution, 1.5 mL, 1.5 mmol) under $N_2$ gas. After being stirred for 30 min, the reaction mixture was quenched by addition of water (0.3 mL) and warmed to rt. The resulting precipitate was filtered off by suction, and the filtrate was dried and evaporated to provide the crude aldehyde **44** (250 mg). $SnCl_4$ (1 M $CH_2Cl_2$ solution, 1.2 mL, 1.2 mmol) was added dropwise to a solution of **14** (300 mg, 1.2 mmol) in dry $CH_2Cl_2$ (5.0 mL) at −78 °C under $N_2$ gas. The reaction mixture was stirred for 30 min, and then a solution of **44** in $CH_2Cl_2$ (2.0 mL) was added. The reaction mixture was warmed to 0 °C, quenched by addition of saturated ammonium chloride solution (1 mL), diluted with water, and extracted with $CH_2Cl_2$. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane−ethyl acetate (1:30 → 1:15) to afford **45** (232 mg, 66%) and *S*-*tert*-butyl (2*S*,3*S*,4*R*,5*R*)-4-(benzyloxy)-5-[(*tert*-butyldimethylsilyl)oxy]-3-hydroxy-2-methoxy-8-methyl-6-nonynethioate (**46**; 20 mg, 7%). The major product **45** was a colorless oil: $[\alpha]^{27}{}_D$ +30.9° (*c* 0.50, $CHCl_3$); MS *m/z* 523 ($M^+$ + 1, 3.0), 311 (19), 255 (82), 211 (41), 183 (19), 91 (100), 73 (27), 57 (31); IR 3570, 2225, 1680 $cm^{-1}$; $^1H$ NMR $\delta$ 7.40−7.25 (m, 5H), 4.97 and 4.65 (ABq, 2H, *J* = 12 Hz), 4.61 (dd, 1H, *J* = 2.0, 8.3 Hz), 4.10 (dd, *J* = 1.0, 8.3 Hz), 3.68 (dd, 1H, *J* = 1.0, 8.3 Hz), 3.49 (d, 1H, *J* = 8.3 Hz), 3.21 (s, 3H), 2.58 (brs, 1H), 2.57 (dhept, 1H, *J* = 2.0, 6.8 Hz), 1.48 (s, 9H), 1.16 (d, 6H, *J* = 6.8 Hz), 0.93 (s, 9H), 0.16 (s, 3H), 0.12 (s, 3H); $^{13}C$ NMR $\delta$ 201.9, 138.4, 128.4, 128.1, 127.7, 93.2, 88.0, 80.3, 78.1, 74.8, 71.7, 65.7, 58.3, 47.5, 29.8, 25.9, 22.7, 22.6, 20.5, 18.2, −4.6, −4.8. Anal. Calcd for $C_{28}H_{46}O_5SSi$: C, 64.32; H, 8.87. Found: C, 64.48; H, 8.90. The minor product **46** was a colorless oil: MS *m/z* 522 ($M^+$, 0.2), 255 (17), 211 (14), 183 (8.0), 125 (3.9), 91 (100), 73 (21), 57 (60); IR 3570, 2225, 1680 $cm^{-1}$; $^1H$ NMR $\delta$ 7.42−7.24 (m, 5H), 4.96 and 4.70 (ABq, 2H, *J* = 11 Hz), 4.62 (dd, 1H, *J* = 2.0, 7.3 Hz), 4.21 (ddd, *J* = 2.9, 5.9, 6.4 Hz), 3.79 (d, 1H, *J* = 5.9 Hz), 3.54 (dd, 1H, *J* = 2.9, 7.3 Hz), 3.49 (s, 3H), 2.77 (d, 1H, *J* = 6.4 Hz), 2.58 (dhept, 1H, *J* = 2.0, 6.8 Hz), 1.48 (s, 9H), 1.16 (d, 6H, *J* = 6.8 Hz), 0.91 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H); $^{13}C$ NMR $\delta$ 201.6, 138.5, 128.2, 127.8, 127.5, 93.0, 88.4, 81.5, 78.1, 74.2, 72.1, 65.4, 59.4, 47.3, 29.8, 25.9, 22.7, 22.7, 20.5, 18.3, −4.6, −4.7. Anal. Calcd for $C_{28}H_{46}O_5SSi$: C, 64.32; H, 8.87. Found: C, 64.46; H, 8.92.

**(2*R*,3*S*,4*R*,5*R*)-4-(Benzyloxy)-3-hydroxy-2-methoxy-5-(3-methyl-1-butynyl)-5-pentanolide (47).** To a solution of **45** (231 mg, 0.44 mmol) in THF (4.0 mL) was added 10% HCl solution (2.0 mL) at 0 °C. After being stirred overnight at rt, the reaction mixture was neutralized by addition of saturated sodium bicarbonate solution and extracted with ethyl acetate. The extract was washed with brine, dried, and concentrated to dryness. Silver(I) trifluoroacetate (500 mg, 2.3 mmol) was added to a solution of the residue in dry THF (5.0 mL). After being heated at 60 °C for 5 h, the reaction mixture was quenched by addition of brine (0.1 mL) at rt and stirred for an additional hour. The precipitate was removed by suction. The filtrate was washed successively with saturated sodium bicarbonate solution and brine, dried, and evaporated. Chromatography of the residue with hexane–ethyl acetate (3:1) gave **47** (113 mg, 80%) as a colorless solid: mp 122.0–123.0 °C (from hexane); $[\alpha]^{25}_{D}$ +93.9° (*c* 0.50, $CHCl_3$); MS *m/z* 275 ($M^+ - C_3H_7$, 6.9), 200 (33), 157 (55), 103 (33), 91 (100), 75 (77), 65 (30); IR 3570, 2225, 1745 cm$^{-1}$; $^1H$ NMR $\delta$ 7.43–7.30 (m, 5H), 5.36 (dd, 1H, $J$ = 2.0, 2.9 Hz), 4.94 and 4.79 (ABq, 2H, $J$ = 12 Hz), 4.29 (t, 1H, $J$ = 3.9 Hz), 4.20 (d, 1H, $J$ = 3.4 Hz), 3.89 (dd, 1H, $J$ = 2.9, 3.9 Hz), 3.66 (s, 3H), 2.95 (brs, 1H), 2.65 (dhept, 1H, $J$ = 2.0, 6.8 Hz), 1.19 (d, 3H, $J$ = 6.8 Hz), 1.19 (d, 3H, $J$ = 6.8 Hz); $^{13}C$ NMR $\delta$ 169.7, 137.2, 128.5, 128.1, 127.9, 95.4, 76.7, 75.8, 73.8, 73.0, 69.5, 69.4, 60.0, 22.4, 20.6. Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.75; H, 7.02.

**4-*O*-Benzyl-6,7,8,9-tetradeoxy-*N*-[(*S*)-hexahydro-2-oxo-1*H*-azepin-3-yl]-8-methyl-2-*O*-methyl-D-*gulo*-6-nonynonamide (48).** A solution of **47** (60 mg, 0.19 mmol), (*S*)-α-amino-ϵ-caprolactam (**12**, 47 mg, 0.37 mmol), and triethylamine (0.05 mL, 0.36 mmol) in THF–dioxane (9:1, 2.0 mL) was stirred overnight. The reaction mixture was concentrated, and the residue was purified by column chromatography with chloroform–methanol (30:1) to give **48** (77 mg, 91%) as a colorless syrup: $[\alpha]^{23}_{D}$ +28.1° (*c* 0.26, $CHCl_3$); MS *m/z* 447 ($M^+$ + 1, 0.5), 349 (26), 331 (23), 241 (36), 200 (51), 177 (31), 155 (37), 91 (100), 84 (40); IR 3400, 2225, 1660 cm$^{-1}$; $^1H$ NMR $\delta$ 7.87 (d, 1H, $J$ = 6.4 Hz), 7.44–7.25 (m, 5H), 6.73 (t, 1H, $J$ = 6.4 Hz), 4.95 and 4.74 (ABq, 2H, $J$ = 11 Hz), 4.68 (brs, 1H), 4.51 (ddd, 1H, $J$ = 1.5, 6.4, 10 Hz), 4.10, (dd, 1H, $J$ = 6.3, 9.8 Hz), 3.97 (d, 1H, $J$ = 6.3 Hz), 3.79 (t, 1H, $J$ = 4.4 Hz), 3.76 (d, 1H, $J$ = 4.4 Hz), 3.40 (s, 3H), 3.12–3.01 (m, 2H), 2.60 (dhept, 1H, $J$ = 2.0, 6.8 Hz), 2.15 (brs, 1H), 2.10–1.24 (m, 6H), 1.17 (d, 6H, $J$ = 6.8 Hz); $^{13}C$ NMR $\delta$ 175.3, 170.3, 138.1, 128.3, 128.1, 127.8, 92.1, 81.1, 80.9, 77.9, 74.9, 72.7, 63.6, 58.3, 52.0, 41.8, 31.0, 28.6, 27.8, 22.7, 20.5; HRMS calcd for $C_{24}H_{34}N_2O_6$ 446.2417, found 446.2427.

**[1(*S*),6*E*]-6,7,8,9-Tetradeoxy-*N*-(hexahydro-2-oxo-1*H*-azepin-3-yl)-8-methyl-2-*O*-methyl-D-*gulo*-6-nonenonamide (Bengamide E, 10).** To a solution of **48** (20 mg, 0.07 mmol) in THF (1.0 mL) were added liquid ammonia (*ca.* 5 mL) and sodium (100 mg, 0.4 mmol) at −78 °C. The reaction mixture was stirred at the same temperature for 1 h. Solid ammonium chloride was added to the reaction mixture, which was then gradually warmed to rt. The residue was taken up in ethyl acetate, which was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with chloroform–methanol (15:1) to furnish **10** (11 mg, 69%) as a colorless oil: $[\alpha]^{22}_{D}$ +24° (*c* 0.1, MeOH) [lit.[8a] $[\alpha]^{29}_{D}$ +25° (*c* 0.29, MeOH]; MS *m/z* 359 ($M^+$ + 1, 0.4), 241 (94), 200 (94), 185 (44), 155 (100), 129 (31), 113 (58), 84 (87); IR 3400, 1660 cm$^{-1}$; $^1H$ NMR $\delta$ 7.97 (d, 1H, $J$ = 5.9 Hz), 6.17 (t, 1H, $J$ = 5.9 Hz), 5.79 (ddd, 1H, $J$ = 1.0, 5.9, 16 Hz), 5.45 (ddd, 1H, $J$ = 1.0, 7.3, 16 Hz), 4.54 (dd, 1H, $J$ = 5.9, 10 Hz), 4.22 (brs, 1H), 3.82 (dd, 1H, $J$ = 1.5, 7.3 Hz), 3.79 (d, 1H, $J$ = 7.3 Hz), 3.60 (dd, 1H, $J$ = 1.5, 5.4 Hz), 3.54 (s, 3H), 3.36–3.22 (m, 2H), 2.37–2.26 (m, 1H), 2.12–1.36 (m, 6H), 1.00 (d, 3H, $J$ = 6.8 Hz), 1.00 (d, 3H, $J$ = 6.8 Hz); $^{13}C$ NMR $\delta$ 174.7, 172.1, 141.8, 125.4, 80.9, 74.3, 72.8, 72.4, 60.0, 52.0, 42.1, 31.1, 30.8, 28.8, 27.9, 22.2, 22.1; HRMS calcd for $C_{17}H_{30}N_2O_6$ 358.2104, found 358.2106.

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**Supporting Information Available:** Copies of the $^{13}C$ NMR spectra of **10** and **48** (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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