

Total Synthesis of Korormicin

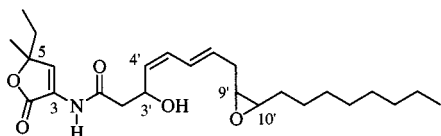
Yuichi Kobayashi,^{*,[a]} Shinya Yoshida,^[a] and Yuji Nakayama^[a]**Keywords:** Borates / Korormicin / Nickel / Total synthesis / Marine natural products

Recently, we have assigned the (5*S*,3'*R*,9'*S*,10'*R*) stereochemistry to planar korormicin (**1**) on the basis of the specific rotations of the four possible diastereoisomers [i.e., (5*S*,3'*R*,9'*S*,10'*R*), (5*S*,3'*S*,9'*S*,10'*R*), (5*S*,3'*S*,9'*R*,10'*S*), and (5*S*,3'*R*,9'*R*,10'*S*) isomers], which were prepared by a total synthesis. In this article, we describe the synthetic aspects in detail. The intermediates in the synthesis are enamino lactone (5*S*)-**4** and both enantiomers of acid **5** and of boronate ester **7**. Lactone (5*S*)-**4** and boronate **7** with (9'*S*,10'*R*) and (9'*R*,10'*S*) chiralities were prepared through asymmetric dihydroxylation of olefins **11** and **30**, respectively, with AD-

mix- α or - β . Compounds (3'*R*)- and (3'*S*)-**5** were prepared by kinetic resolution of *rac*-**19** with asymmetric epoxidation. Condensation of (5*S*)-**4** and (3'*R*)- or (3'*S*)-**5** with DCC in the presence of DMAP and PPTS furnished the advanced intermediate **6** with (5*S*,3'*R*) and (5*S*,3'*S*) chiralities in good yields. Addition of PPTS was important to prevent formation of acyl urea **24**. A nickel-catalyzed coupling reaction between **6** and **8** [prepared in situ from (9'*S*,10'*R*)- or (9'*R*,10'*S*)-**7** and MeLi] produced **9**, which upon deprotection with Bu₄NF furnished the four diastereoisomers of korormicin (**1**).

Introduction

Recently, Yoshikawa isolated korormicin from the bacterium *Pseudoalteromonas* sp. F-420. Korormicin has an inhibitory activity towards the growth of marine Gram-negative bacteria, whereas it is inactive against terrestrial microorganisms.^[1] According to the authors, this unique activity and specificity are of a sufficient level for use as a probe for the classification of unidentified marine bacteria. In addition, korormicin could be of use as a lead compound in the development of effective drugs for fish in aquaculture against diseases caused by Gram-negative bacteria. The planar structure and geometries of the diene and the epoxide parts of korormicin were determined by the authors on the basis of NMR and MS data as depicted in **1** (Figure 1).^[1a] Consequently, clarification of the proposed structure and the absolute configuration was an urgent issue in order to develop the potential of korormicin.

Figure 1. Planar structure of korormicin (**1**)

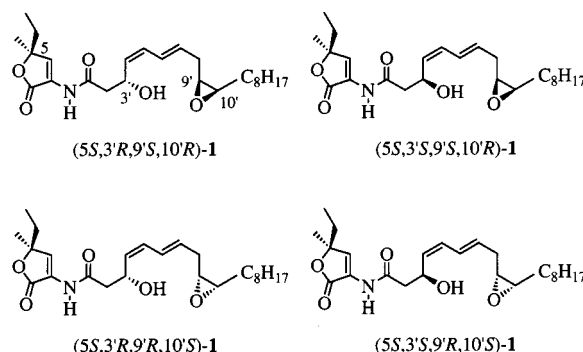
Recently, we^[2] and another group^[3] have succeeded in the determination of the chiral centers in korormicin. In our investigation, a stereoselective synthesis of korormicin was first developed, and then the specific rotations of the four possible diastereoisomers were compared with the reported value for natural korormicin {[α]_D²⁶ = -24.4 (c = 0.29,

EtOH)}.^[1a] The construction of the chiral centers of the conjugated diene and the enamino lactone moiety is highly efficient, and hence all of the stereoisomers can be obtained stereospecifically. Herein, we would like to describe the synthesis in detail.

Results and Discussion

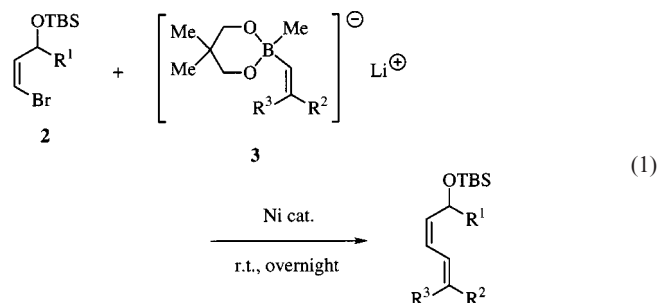
Strategy for the Synthesis

Since natural korormicin was not available to us, we used the spectroscopic data (¹H NMR and ¹³C NMR taken in [D₆]DMSO) and the specific rotation data published by Yoshikawa. Eight stereoisomers exist in total for korormicin, and therefore four signals from any proton(s) and/or carbon atom(s) should be detected separately in the NMR spectra in order to differentiate the four possible diastereoisomers. We examined this by means of the NMR spectra of korormicin synthesized as a diastereoisomeric mixture from racemic fragments. In addition, the diastereoisomers listed in Figure 2 were selected for comparison of their [α]_D values with that of natural korormicin.

Figure 2. Possible stereoisomers of (5*S*)-korormicin

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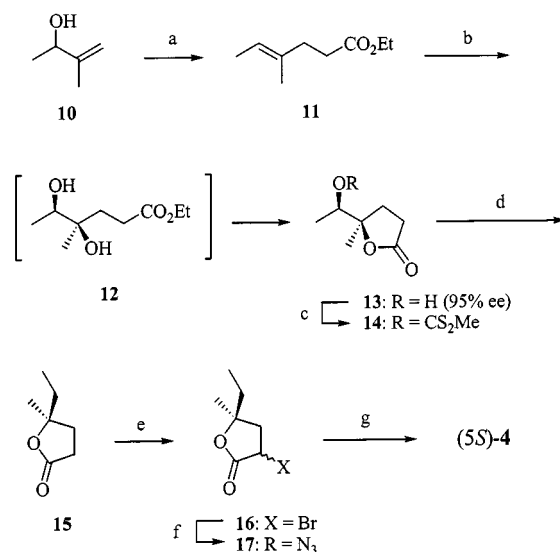
Recently, we reported a nickel-catalyzed coupling reaction between bulky alkenyl halides **2** and alkenyl borates **3** [Equation (1)],^[4] and the reaction was applied to the construction of the key intermediates in the synthesis of 10,11-dihydroleukotriene B₄ and related compounds.^[5] The reactivity and the almost neutral character of the borates are synthetic advantages of this reaction.^[6,7] Accordingly, we envisioned a sequence as in Scheme 1 to synthesize the diastereoisomers of korormicin (Figure 2). In the following paragraphs, preparation of the requisite intermediates and synthesis of korormicin are described.



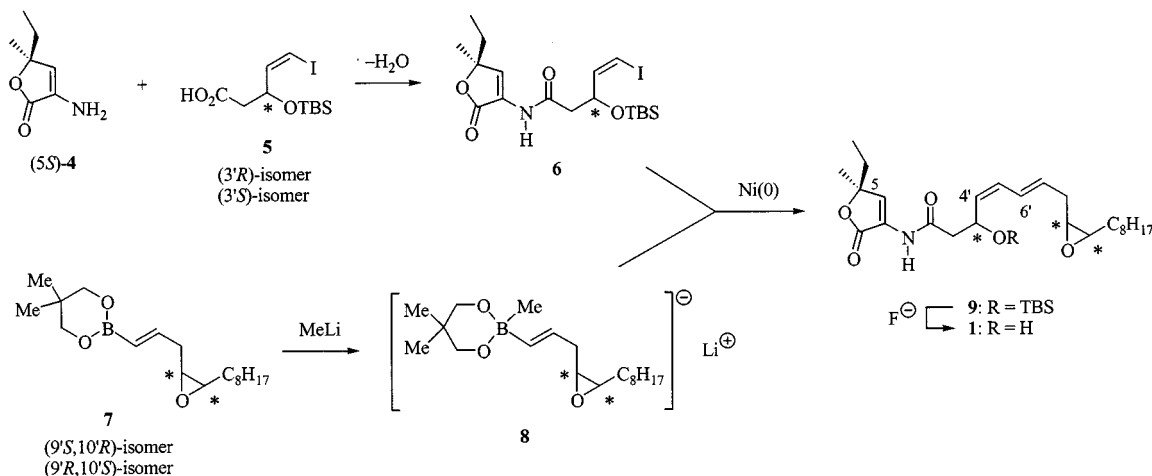
Synthesis of the Key Intermediates

Synthesis of enaminolactone (5*S*)-**4** was accomplished successfully by a route summarized in Scheme 2^[8] in which the crucial step is construction of the enamine moiety onto the lactone **15** by the method of Kraatz.^[9] The Johnson–Claisen rearrangement of **10** with MeC(OEt)₃ at 150 °C afforded ester **11** stereoselectively.^[10] Asymmetric dihydroxylation^[11] (AD) of **11** with AD-mix-β produced diol **12**,^[12] which under the given basic conditions underwent lactonization to yield lactone **13** with 95% ee^[13] in good yield. The hydroxy group in **13** was transformed into the xanthate ester moiety, and the latter was removed under radical conditions^[14] to afford lactone **15** in 75% yield from **11**.^[15] Attempted bromination of **15** with the method of Kraatz^[9] (Br₂ and PBr₃ at 130 °C) gave a complex mixture,

whereas reaction of the lithium enolate derived from **15** and LDA with CBr₄ at –78 °C resulted in dibromination. This is certainly caused by the fast proton transfer of α-bromolactone **16** to the enolate anion derived from lactone **15** compared with the slow nucleophilic reaction of the enolate with CBr₄. Accordingly, nonnucleophilic conditions were examined, that is, enolate trapping of the lithium enolate with TMSCl followed by reaction with Br₂. Fortunately, the reaction proceeded cleanly at –78 °C as monitored by TLC to furnish α-bromolactone **16**, which was a 1:1 diastereoisomeric mixture by ¹H NMR spectroscopy. Subsequently, reaction of **16** with NaN₃ in refluxing EtOH overnight afforded azide **17** which, upon treatment with NaOEt (0.1 equiv.) in EtOH, produced **4** in 58% yield from lactone **15**.

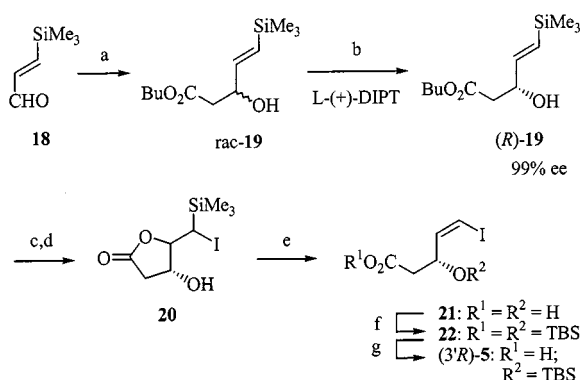
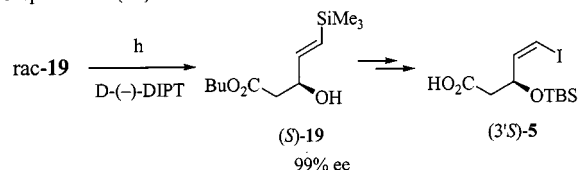


Scheme 2. (a) MeC(OEt)₃ (5 equiv.), EtCO₂H (10 mol-%), 150 °C, 3 d (81%); (b) AD-mix-β, MeSO₂NH₂, *t*BuOH/H₂O, 0 °C; (c) CS₂, imidazole (cat.), NaH, THF then MeI (82% from **11**); (d) Bu₃SnH, AIBN (cat.), toluene, reflux (92%); (e) (i) LDA, THF, –78 °C, (ii) TMSCl, (iii) Br₂; (f) NaN₃, EtOH; (g) NaOEt, EtOH (58% from **15**)



Scheme 1. Strategy for synthesis of (5*S*)-korormicin

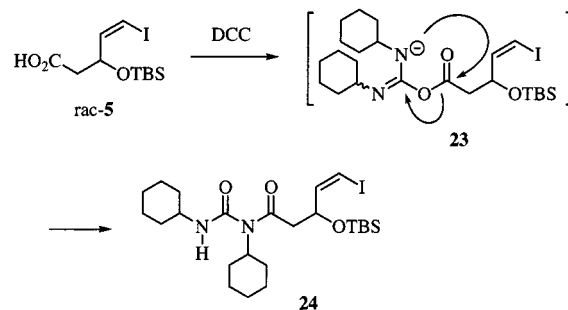
Preparation of (3'*R*)-**5** was previously reported by Sato as a communication (Scheme 3).^[16] The key alcohol (*R*)-**19** in his synthesis is prepared by the kinetic resolution of *rac*-**19** using the Sharpless reagent^[17] [*t*BuOOH, Ti(OPr)₄, L-(+)-diisopropyl tartrate (L-(+)-DIPT)]. In our research, (*R*)- as well as (*S*)-**19** with 99% *ee* were prepared in 38% and 40% yields based on *rac*-**19** with L-(+)- or D-(−)-DIPT, respectively. Both enantiomers of **19** were transformed into (3'*R*)- and (3'*S*)-**5** in good yields without any problems.

Preparation of (3'*R*)-**5**Preparation of (3'*S*)-**5**

Scheme 3. (a) LiCH₂CO₂Bu, −78 °C (93%); (b) *t*BuOOH, Ti(OPr)₄, L-(+)-DIPT, −20 °C (38%); (c) 1 N NaOH, THF/Et₂O/MeOH (1:1:1); (d) I₂, NaHCO₃ aq., THF/Et₂O/MeOH (1:1:1) [94% from (*R*)-**19**]; (e) Bu₄NF, THF, −10 °C; (f) TBSCl, imidazole, DMF; (g) K₂CO₃, MeOH, room temp., 1 h (78% from **20**); (h) *t*BuOOH, Ti(OPr)₄, D-(−)-DIPT, −20 °C (40%)

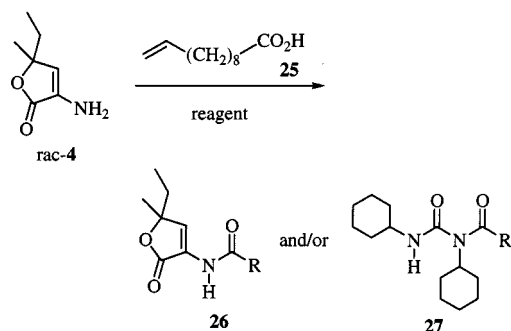
The reaction conditions for DCC condensation to yield amide **6** (Scheme 1) were explored by using the racemic partners, that is, enamine *rac*-**4** and acid *rac*-**5**, as it was feared that the intramolecular attack of the nitrogen anion of **23** on to the carbonyl carbon atom would produce the acyl urea **24** as a by-product (Scheme 4). In practice, the amide **6** was produced in 84% yield by means of the procedure of Steglich^[18] [DCC (1.2 equiv.) and 4-dimethylaminopyridine (DMAP, 0.2 equiv.) in CH₂Cl₂] with approximately 10% of the acyl urea **24**,^[19] and these products were inseparable by chromatography on silica gel. To make matters worse, transformation of **6** to diene **9** and subsequently to korormicin (**1**) was contaminated by the compounds derived from urea **24**, as compound **24** and amide **6** have the same iodovinyl moiety. Chromatographic separations of the desired products (**9** and **1**) and the by-products after the coupling reaction and after the subsequent deprotection were found to be difficult.

In order to circumvent this situation, condensation of *rac*-**4** and acid **25** was studied as a model system [Equation (2)]. The conditions of Steglich^[18] (DCC/DMAP) fur-



Scheme 4

nished the desired amide **26** and the acyl urea **27** in a ratio of 9:1, a similar result to that described above. Formation of such acyl ureas was reported by Keck^[20] in their macro-lactonization and intermolecular esterification under high-dilution conditions. The problem was solved by addition of DMAP·HCl which efficiently delivers a proton to the nitrogen anion before the rearrangement. This idea has also been applied successfully in the synthesis of macrophelides with camphorsulfonic acid (CSA).^[21] In our case, the condensation partner **4** is not an alcohol but an amine. Consequently, it seemed important to find a selective acid, which efficiently quenches the nitrogen anion in **23** before the rearrangement and which does not protonate the nitrogen atom in **4**. With *p*TsOH or CSA, the reaction did not take place, while the mild acid PPTS (0.3–0.5 equiv.) produced **26** in 63% yield without contamination with **27**. Other reagents such as DCC/HOSu, EDC·HCl in CH₂Cl₂ or DMF, EDC·HCl/Et₃N in CH₂Cl₂ or DMF, (EtO)₂P(=O)CN, and 2-Cl-N(Me)-Py⁺·I[−] did not afford amide **26** perhaps because of the low reactivity of the intermediate toward the nitrogen atom in **4**, which is of low nucleophilicity due to the conjugation of the enamine moiety with the carbonyl group. The above conditions with PPTS were then applied to the real partners [i.e., (*5S*)-**4** with (3'*R*)- or (3'*S*)-**5**], and (*5S*,3'*R*)- and (*5S*,3'*S*)-**6** were obtained as sole products in 82% and 76% yields, respectively. Similarly, *rac*-**4** and **5** produced **6** as a diastereomeric mixture in 70% yield.



Reagent	Result
DCC/DMAP	26 + 27 (9 : 1)
DCC/DMAP/ <i>p</i> -TsOH·H ₂ O	No reaction
DCC/DMAP/CSA	No reaction
DCC/DMAP/PPTS	26 (63%)

R : (CH₂)₈CH=CH₂

Both enantiomers of boronate ester **7** were prepared according to the sequence illustrated in Scheme 5, the necessary chiral centers were constructed on olefin **30** by using AD-mix- α or - β .^[11] Nonanal (**28**) was converted into alcohol **29** in 89% yield^[22] by Wittig reaction with $(\text{EtO})_2\text{P}(=\text{O})\text{CH}_2\text{CO}_2\text{Et}$ followed by reduction with DIBAL. Chlorination^[23] of allylic alcohol **29** and subsequent dihydroxylation of **30** using AD-mix- α afforded *syn*-diol **31** in good yield. Without purification, **31** was exposed to crushed NaOH in THF to produce epoxy alcohol **32** in 90% *ee*.^[13] Mesylation of **32** and subsequent epoxide ring opening^[24] with the reagent derived from $\text{TMSC}\equiv\text{CLi}$ and $\text{BF}_3\cdot\text{OEt}_2$ gave the unstable acetylenic alcohol **34** which, on treatment with K_2CO_3 in MeOH, underwent the epoxide ring formation and, concomitantly, desilylation to produce epoxide **35** in 69% yield from epoxy alcohol **32**. Transformation of the acetylenic part of **35** into the vinyl-boronate moiety was accomplished stereoselectively by hydroboration with $(\text{Ipc})_2\text{BH}$ (Ipc: isopinocampheyl) followed by oxidation with excess MeCHO according to the Suzuki–Miyaura reaction.^[25] Ligand exchange of the resulting diethyl boronate ester **36** with 2,2-dimethyl-1,3-propanediol furnished (9'*S*,10'*R*)-**7** in 64% yield from epoxide **35**.

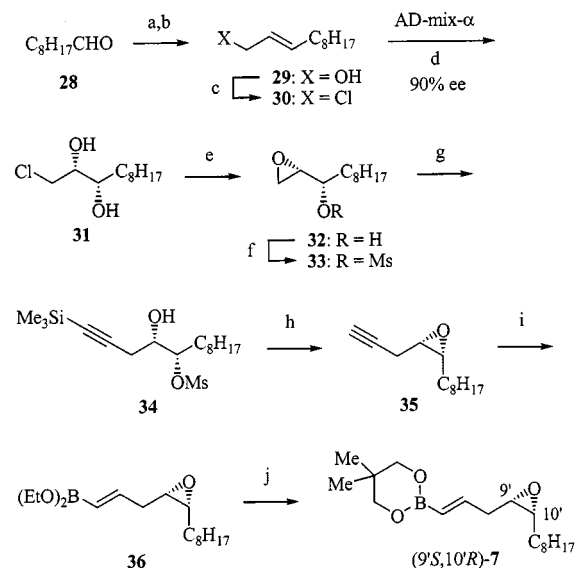
The synthesis of (9'*R*,10'*S*)-**7** was performed with the same methodology through epoxide *ent*-**32** derived from diol *ent*-**31** which, in turn, was prepared by AD reaction of olefin **30** using AD-mix- β . The enantiomeric purity of epoxide *ent*-**32** was > 99% *ee*.^[13] In addition, racemic diol *rac*-**31** was prepared from **30** with OsO_4 (cat.) and NMO in 95% yield, and was transformed into racemic epoxide *rac*-**7** (structures of *rac*-**31** and -**7** are not shown).

Synthesis of Korormicin

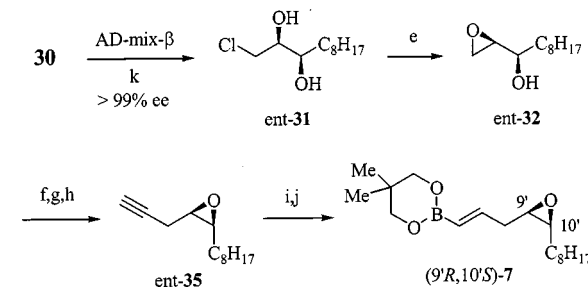
We were now ready for the coupling reaction proposed in Scheme 1 to furnish korormicin (**1**). First, the racemic intermediates were used in order to examine the reaction conditions and to check whether the NMR method mentioned above met our requirements. Concomitant transformation of boronate ester *rac*-**7** (1.4 equiv. per **6**) and $\text{NiCl}_2(\text{PPh}_3)_2$ (15 mol-%) into lithium borate *rac*-**8** and a Ni^0 catalyst was effected by addition of MeLi (1.6 equiv.) (0 °C, 15 min) and a subsequent coupling reaction with a diastereoisomeric mixture of iodide **6** at room temperature as described before^[4] to afford diene **9**. No contamination of the geometric isomers or formation of other by-product(s) which might be produced by attack of MeLi on the epoxide function of **7** occurred. The *cis,trans* geometry of the diene was confirmed by the coupling constants in the ^1H NMR spectrum: $J_{4'-5'} = 11$ Hz, $J_{6'-7'} = 15$ Hz. Finally, reaction of **9** with Bu_4NF induced deprotection to afford **1** as a mixture of diastereoisomers in 35% yield from iodide **6**. The ^1H (300 MHz) and ^{13}C NMR spectra of synthetic product **1** in $[\text{D}_6]\text{DMSO}$ were fully consistent with the data reported for natural **1**.^[1a]

We then carefully scanned the expanded spectra of **1** in $[\text{D}_6]\text{DMSO}$ and CDCl_3 and those of **9** in CDCl_3 to find any signals of proton(s) and/or carbon atom(s) clearly re-

Preparation of (9'*S*,10'*R*)-**7**



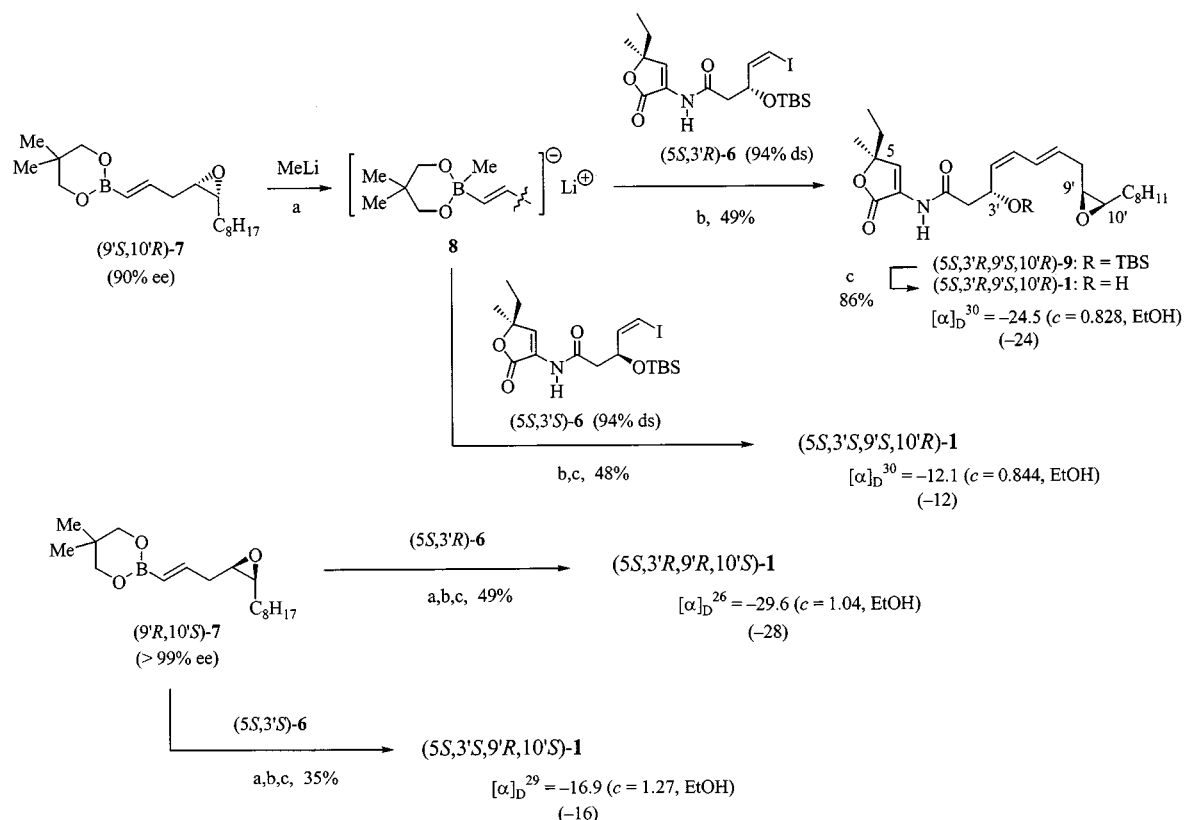
Preparation of (9'*S*,10'*S*)-**7**



Scheme 5. (a) $(\text{EtO})_2\text{P}(=\text{O})\text{CH}_2\text{CO}_2\text{Et}$, NaH, THF; (b) DIBAL, -70 °C (89% from **28**); (c) CCl_4 , PPh_3 (81%); (d) AD-mix- α , MeSO_2NH_2 , 0 °C; (e) NaOH (5 equiv.), THF, room temp., 30 min (**32**, 84% from **30**; *ent*-**32**, 73%); (f) MsCl , NEt_3 , CH_2Cl_2 , 0 °C; (g) (i) $\text{TMSC}\equiv\text{CH}$ (1.7 equiv.), $n\text{BuLi}$ (1.5 equiv.), (ii) $\text{BF}_3\cdot\text{OEt}_2$ (1.7 equiv.), -78 °C, (iii) **33**, -78 °C, 30 min; (h) K_2CO_3 (3 equiv.), MeOH, room temp., 4 h (**35**, 69% from **32**; *ent*-**35**, 58% from *ent*-**32**); (i) $(\text{Ipc})_2\text{BH}$ (1.2 equiv.), THF, then MeCHO (15 equiv.), 40 °C (reflux), overnight; (j) $\text{HOCH}_2\text{C}(\text{Me})_2\text{CH}_2\text{OH}$, THF [(9'*S*,10'*R*)-**7**, 64% from **35**; (9'*R*,10'*S*)-**7**, 76% from *ent*-**35**]; (k) AD-mix- β , MeSO_2NH_2 , 0 °C

solved into four peaks corresponding to the four diastereoisomers. Several carbon atom signals of **1** and **9** in the ^{13}C NMR spectra and the C(5) methyl proton signals of **9** in ^1H NMR spectrum were actually resolved, but only into two lines with $\Delta\delta < 0.2$ ppm for the carbon atoms and < 0.02 ppm for the protons. These results indicate that the NMR approach at 300 MHz (for ^1H) is insufficient for determination of the stereochemistry.

Next, the synthesis of the diastereoisomers listed in Figure 2 was carried out with the enantiomerically enriched intermediates prepared in Schemes 3, 5, and 6 for the second study, that is, a comparison of their $[\alpha]_D$ values with that for natural korormicin. The results are summarized in Scheme 6.



Scheme 6. Synthesis of the four diastereoisomers of **1**; specific rotations are calculated from the measured $[\alpha]_D$ values shown in parentheses based on the (*R*)/(*S*) chirality ratio at each of the chiral centers: (a) **7** (1.5 equiv. based on **6**), MeLi (1.8 equiv.), $\text{NiCl}_2(\text{dppf})$ (10–15 mol-%), THF, 0 °C, 15 min; (b) **6**, room temp., 4 h (46–56% based on **6**); (c) Bu_4NF (2 equiv.), THF, room temp., 30 min (76–94%)

Since the stereoisomeric purity of boronate esters **7** and iodide **6** did not exceed 99%, the measured $[\alpha]_D$ values given in the parentheses are corrected for the pure stereoisomers by a linear calculation of the measured values after consideration of the (*R*)/(*S*) chirality ratio at each of the chiral centers. The value obtained from the (*5S,3'R,9'S,10'R*) isomer (–24.5) is the closest to that for natural korormicin (–24.4)^[1a] and all the other values are outside the range of error of ± 2 degrees; hence, this isomer is the natural korormicin.

Conclusion

In summary, the synthesis of korormicin has been established. The three key intermediates shown in Scheme 1 have been prepared efficiently by the AD reaction of **11** and **30** with AD-mix- α and/or $-\beta$ or the kinetic resolution of *rac*-**19** using asymmetric epoxidation to give high enantiomeric excess of 95% for (*5S*)-**4**, 99% for (*3'R*)- and (*3'S*)-**5**, 90% for (*9'S,10'R*)-**7**, and > 99% for (*9'R,10'S*)-**7**. Other olefins with similar structures to **11**, *rac*-**19**, and **30** may also undergo these key reactions to provide synthetic analogues of **1**, and give useful compounds useful in the research field(s) of biochemistry. In addition, the construction of the diene by coupling reaction of iodide **6** and boronate ester **7** with the Ni catalyst demonstrates the potential usefulness of this

reaction for the synthesis of sterically congested conjugated olefin systems frequently seen in other natural products such as fostriecin and didemnilactone.

Experimental Section

General: The following solvents were distilled before use: THF (from Na/benzophenone), Et_2O (from Na/benzophenone), and CH_2Cl_2 (from CaH_2). *N,N*-Dimethylformamide (DMF) was dried with CaH_2 . Routinely, organic extracts were dried with MgSO_4 and concentrated using a rotary evaporator to leave residues, which were purified by chromatography on silica gel purchased from Merck (Silicagel 60). – Infrared (IR) spectra are reported in wave numbers (cm^{-1}). – The ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured in CDCl_3 with SiMe_4 ($\delta = 0$) and the center line of CDCl_3 triplet ($\delta = 77.1$) as internal standards, respectively.

Ethyl (*E*)-Methylhex-4-enoate (11**):** To an ice-cold solution of MeMgI in Et_2O (67 mL, 1.98 M, 133 mmol), methacrolein (8.47 g, 121 mmol), dissolved in Et_2O (60 mL), was added dropwise. After the addition, the solution was stirred at 0 °C for 30 min and the mixture was poured into a mixture of 1 N HCl and Et_2O . The layers were separated, and the aqueous layer was extracted with Et_2O . The combined extracts were washed with NaHCO_3 and dried. The solvent was removed by distillation at 1 atm to leave a residue which was distilled at reduced pressure to afford **10** (8.3 g, 80%). – B.p. 70 °C (50 Torr). – ^{13}C NMR: $\delta = 149.1, 109.6, 71.6, 21.6$,

17.8. – The ^1H NMR spectrum is identical with that reported^[10] and is updated: δ = 1.25 (d, J = 7 Hz, 3 H), 1.72 (s, 3 H), 1.9 (br. s, 1 H), 4.20–4.25 (m, 1 H), 4.76 (s, 1 H), 4.93 (s, 1 H). – A mixture of 3-methyl-2-butanol (**10**) (7.5 g, 87 mmol), $\text{MeC}(\text{OEt})_3$ (70.8, 436 mmol), and EtCO_2H (650 mg, 8.6 mmol) in a sealed tube was stirred at 150 °C for 3 d and poured into 1 N HCl. The resulting mixture was extracted with EtOAc three times, and the combined extracts were dried and concentrated to afford a residue, which was distilled to give **11** (11.02 g, 81%). – B.p. 130 °C (20 Torr) [ref.^[10] 90 °C (0.5 Torr)]. – The ^1H NMR spectrum of the product is identical with the data reported.^[10] – ^{13}C NMR: δ = 173.8, 134.2, 119.4, 60.3, 34.7, 33.2, 15.5, 14.2, 13.3.

S-Methyl (1*R*,2'*R*)-O-[1-(2'-Methyl-5'-oxotetrahydrofuran-2-yl)-ethyl]dithiocarbonate (14**):** To an ice-cold mixture of AD-mix- β (27 g) and MeSO_2NH_2 (1.83 g, 19.2 mmol) in *t*BuOH (100 mL) and H_2O (100 mL), **11** (3.00 g, 19.2 mmol) was added dropwise. The mixture was stirred at 0 °C overnight and the excess reagent was destroyed with NaHSO_3 (25 g, 240 mmol). The resulting mixture was extracted twice with EtOAc and the combined extracts were dried and concentrated. The residue was semi-purified after passage through a short column of silica gel first with hexane and then with CHCl_3 to afford lactone **13**, 95% *ee* by ^1H NMR spectroscopy of the derived MTPA ester. Product **13** was used for the next reaction without further purification, and an analytically pure sample was obtained by chromatography (hexane/EtOAc). – ^1H NMR: δ = 1.23 (d, J = 6 Hz, 3 H), 1.37 (s, 3 H), 1.86–1.98 (m, 1 H), 2.20–2.32 (m, 1 H), 2.32–2.54 (m, 1 H), 2.56–2.73 (m, 2 H), 3.71–3.80 (m, 1 H). – ^{13}C NMR: δ = 177.3, 88.9, 72.9, 30.5, 29.3, 21.1, 17.0. – To an ice-cold solution of the above lactone **13**, CS_2 (4.41 g, 57.9 mmol), and imidazole (65 mg, 0.95 mmol) in THF (40 mL), NaH (1.7 g, 50% suspension in mineral oil, 35 mmol) was added in portions. The ice/water bath was removed and stirring was continued for 1 h. The mixture was immersed into an ice/water bath again, and MeI (6.84 g, 48.2 mmol) was added. The resulting mixture was stirred at room temperature for 30 min and poured into saturated NH_4Cl with EtOAc. The product was extracted with EtOAc repeatedly, and the combined extracts were dried and concentrated to give a residue which was purified by chromatography (hexane/EtOAc) to afford **14** (3.69 g, 82% from **11**). – $[\alpha]_D^{29}$ = +49 (c = 0.86, CHCl_3). – IR (nujol): $\tilde{\nu}$ = 1759, 1045 cm^{-1} . – ^1H NMR: δ = 1.39 (d, J = 7 Hz, 3 H), 1.46 (s, 3 H), 2.00 (ddd, J = 13 Hz, 10, 8 Hz, 1 H), 2.23 (ddd, J = 13 Hz, 10, 6 Hz, 1 H), 2.56 (s, 3 H), 2.48–2.73 (m, 2 H), 5.77 (q, J = 6.5 Hz, 1 H). – ^{13}C NMR: δ = 215.7, 176.6, 86.4, 83.7, 31.1, 29.1, 23.9, 19.2, 13.9.

(S)-4-Methyl-4-hexanolide (15**):** A mixture of **14** (3.98 g, 17.0 mmol), Bu_3SnH (7.45 g, 25.5 mmol), and AIBN (30 mg, 0.18 mmol) in toluene (200 mL) was stirred overnight under reflux and concentrated to leave an oil, which was purified by chromatography (hexane/EtOAc) followed by distillation to afford **15** (2.0 g, 92%). – B.p. 150 °C (10 Torr). – $[\alpha]_D^{29}$ = –9.5 (c = 0.80, CHCl_3). – IR (neat): $\tilde{\nu}$ = 1770, 1165, 937 cm^{-1} . – ^1H NMR: δ = 0.93 (t, J = 7.5 Hz, 3 H), 1.34 (s, 3 H), 1.56–1.77 (m, 2 H), 1.94 (ddd, J = 13 Hz, 10, 7 Hz, 1 H), 2.04 (ddd, J = 13 Hz, 10, 9 Hz, 1 H), 2.53 (ddd, J = 18, 9, 7 Hz, 1 H), 2.60 (ddd, J = 18, 9, 8 Hz, 1 H). – ^{13}C NMR: δ = 177.1, 87.2, 33.5, 32.3, 29.1, 25.0, 8.0. – $\text{C}_7\text{H}_{12}\text{O}_2$ (128.2): calcd. C 65.60, H 9.44; found C 65.31, H 9.48.

(S)-2-Aminohex-2-en-4-olide [(5*S*)-4**]:** To an ice-cold solution of *i*Pr₂NH (1.78 g, 17.6 mmol) in THF (15 mL) was added *n*BuLi (6.2 mL, 2.26 M in hexane, 14 mmol). The solution was stirred for 30 min, and then cooled to –78 °C, and lactone **15** (1.50 g, 11.7 mmol) was added. The solution was stirred at –78 °C for a further 1 h, and then TMSCl (1.91 g, 17.6 mmol) was added. The

resulting mixture was warmed up to 0 °C over 1 h to produce the silyl enol ether, which was used for the next reaction without isolation. – The above solution was cooled again to –78 °C and Br_2 (2.23 g, 14.0 mmol) was added. The mixture was allowed to warm up to room temperature over 30 min and then the solution was poured into a mixture of saturated NaHCO_3 and EtOAc with vigorous stirring. The organic layer was separated and the aqueous layer was extracted with EtOAc three times. The combined organic layers were washed with aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and dried. Evaporation of the solvents gave a residue which was semi-purified by chromatography (hexane/EtOAc) to afford α -bromolactone **16**. – IR (neat): $\tilde{\nu}$ = 1770, 945 cm^{-1} . – ^1H NMR: δ = 0.95 and 0.98 (2t, J = 7.5 and 7.5 Hz, 3 H), 1.37 and 1.55 (2s, 3 H), 1.60–1.95 (m, 2 H), 2.37 and 2.44 (2dd, J = 14, 6 and 15, 8 Hz, 1 H), 2.64 and 2.76 (2dd, J = 14, 9 and 15, 9 Hz, 1 H), 4.57 and 4.64 (2dd, J = 9, 6 and 9, 8 Hz, 1 H). – ^{13}C NMR: δ = 172.7 and 172.5, 87.0 and 86.8, 43.4 and 43.1, 38.2 and 38.0, 34.1 and 33.8, 25.7 and 25.1, 8.02 and 7.99. – A mixture of the above bromide, NaN_3 (2.28 g, 35.1 mmol), and EtOH (20 mL) was stirred overnight under reflux and filtered through a pad of Celite with EtOAc. The filtrate was concentrated to give a residue, which was diluted with brine. The resulting mixture was extracted three times with EtOAc. The combined extracts were dried and concentrated to afford a somewhat unstable α -azidolactone **17**, which was used for the next reaction without further purification. – To a solution of NaOEt in EtOH, prepared from sodium (50 mg, 0.0022 g-atom) and EtOH (20 mL), was added a solution of unpurified **17**, dissolved in EtOH (10 mL). After 30 min of stirring at room temperature, the solvent was removed by evaporation to give a residue, which was suspended in saturated NH_4Cl . The resulting mixture was extracted three times with EtOAc, and the combined organic layers were dried and concentrated. The residual viscous oil was purified by chromatography (hexane/EtOAc) to afford enaminalactone (5*S*)-**4** (0.96 g, 58% from **15**). – $[\alpha]_D^{26}$ = –25 (c = 0.96, CHCl_3). – IR (nujol): $\tilde{\nu}$ = 3448, 3359, 1739, 1668 cm^{-1} . – ^1H NMR: δ = 0.82 (t, J = 7.5 Hz, 3 H), 1.38 (s, 3 H), 1.58–1.81 (m, 2 H), 3.71 (br. s, 2 H), 5.79 (s, 1 H). – ^{13}C NMR: δ = 170.8, 132.6, 119.7, 86.5, 32.5, 24.9, 8.1. – $\text{C}_7\text{H}_{11}\text{NO}_2$ (141.2): calcd. C 59.56, H 7.85; found C 59.80, H 7.85.

Butyl (E)-3-Hydroxy-5-trimethylsilyl-4-pentenoate (*rac*-19**):** To an ice-cold solution of *i*Pr₂NH (2.86 g, 28.2 mmol) in THF (50 mL) was added *n*BuLi (10.3 mL, 2.50 M in hexane, 25.8 mmol). The mixture was stirred for 15 min, and then the solution was cooled to –78 °C and *n*-butyl acetate (3.00 g, 25.8 mmol) was added. The solution was stirred at –78 °C for 30 min, and aldehyde **18**^[26] (3.00 g, 23.4 mmol) was added. The resulting solution was stirred at –78 °C for 10 min and poured into a mixture of Et₂O and saturated NH_4Cl with vigorous stirring. The layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layers were dried and concentrated to leave an oil, which was purified by chromatography to afford alcohol *rac*-**19** (5.32 g, 93%). – IR (neat): $\tilde{\nu}$ = 3448, 1738, 867, 839 cm^{-1} . – ^1H NMR: δ = 0.05 (s, 9 H), 0.92 (t, J = 7 Hz, 3 H), 1.36 (sext, J = 7 Hz, 2 H), 1.60 (quint, J = 7 Hz, 2 H), 2.48 (dd, J = 16, 8 Hz, 1 H), 2.58 (dd, J = 16, 4 Hz, 1 H), 3.03 (d, J = 5 Hz, 1 H), 4.10 (t, J = 7 Hz, 1 H), 4.45–4.55 (m, 1 H), 5.93 (dd, J = 19, 1 Hz, 1 H), 6.03 (dd, J = 19, 4 Hz, 1 H). – ^{13}C NMR: δ = 172.7, 146.0, 130.5, 70.4, 64.7, 41.0, 30.6, 19.1, 13.6, –1.50.

Kinetic Resolution of *rac*-19**:** To a solution of $\text{Ti}(\text{O}i\text{Pr})_4$ (5.83 g, 20.5 mmol) in CH_2Cl_2 (200 mL) at –20 °C was added L-(+)-DIPT (5.77 g, 24.6 mmol). The solution was stirred at –20 °C for 10 min, and *rac*-**19** (5.01 g, 20.5 mmol) was added to the solution. Stirring was continued at –20 °C for 10 min, and *t*BuOOH (6.5 mL, 4.74

m in CH_2Cl_2 , 30.8 mmol) was added slowly to the solution. The solution was left at -20°C overnight and the reaction was terminated by the addition of Me_2S (4.4 g, 68 mmol). After 30 min at -20°C , 10% aqueous tartaric acid (20 mL), NaF (20 g, 476 mmol), and Celite (20 g) were added to the solution. The resulting mixture was stirred at room temperature overnight and filtered through a pad of Celite with Et_2O . The filtrate was concentrated and the residue was purified by chromatography to afford (*R*)-**19** (1.90 g, 38% based on *rac*-**19**), which was 99% *ee* by ^1H NMR spectroscopy of the derived MTPA ester.

(3*R*,4*R*,5*R*)- and (3*R*,4*S*,5*S*)-3-Hydroxy-5-iodo-5-trimethylsilyl-4-pentanolide (20): A mixture of alcohol (*R*)-**19** (1.49 g, 6.10 mmol), THF (6 mL), Et_2O (6 mL), MeOH (6 mL), and 1 N NaOH (9.0 mL, 9.0 mmol) was stirred at room temperature overnight and 1 N HCl (ca. 15 mL) was added dropwise until the solution became acidic. The mixture was extracted with CHCl_3 repeatedly and the combined organic layers were dried and concentrated to furnish the corresponding acid, which was used for the next reaction without further purification. – To an ice-cold mixture of the above acid, THF (6 mL), Et_2O (6 mL), MeOH (6 mL), and saturated NaHCO_3 (15 mL), crushed I_2 (2.33 g, 9.2 mmol) was added. The mixture was stirred at 0°C for 30 min and poured into a mixture of CHCl_3 and aqueous $\text{Na}_2\text{S}_2\text{O}_3$. The layers were separated, and the aqueous layer was extracted with CHCl_3 three times. The combined organic layers were dried and concentrated to give a yellow solid, which was purified by chromatography to furnish iodolactone **20** [1.80 g, 94% from (*R*)-**19**] as a diastereomeric mixture. – ^1H NMR: δ = 0.22 (s, 9 H), 2.48 and 2.59 (dd and d, J = 19, 4 and 18 Hz, 1 H), 2.77 and 2.97 (2dd, J = 18, 5 and 19, 8 Hz, 1 H), 3.09 and 3.59 (2d, J = 5 and 5 Hz, 1 H, OH), 3.28 and 3.39 (2d, J = 6 and 12 Hz, 1 H), 4.31 and 4.51 (2dd, J = 6, 3 and 12, 3 Hz, 1 H), 4.37–4.45 and 4.68–4.74 (2m, 1 H). – ^{13}C NMR: δ = 176.5 and 175.5, 88.3 and 85.8, 72.5 and 69.3, 39.0 and 38.5, 20.5 and 12.3, –1.14 and –1.37.

(3*R*,4*Z*)-[3-(*tert*-Butyldimethylsilyloxy)-5-iodo-4-pentenoic Acid [(3'*R*)-5**]:** To a solution of lactone **20** (1.51 g, 4.81 mmol) in THF (20 mL) was added dropwise TBAF (7.2 mL, 1.0 M in THF, 7.2 mmol) at -10°C . The solution was stirred at -10°C for 1 h and poured into a mixture of CHCl_3 and 1 N HCl with vigorous stirring. The layers were separated and the aqueous layer was extracted with CHCl_3 repeatedly. The combined organic layers were dried and concentrated to afford acid **21** as a viscous oil, which was used for the next reaction without further purification. – A mixture of acid **21**, TBSCl (1.84 g, 12.2 mmol), imidazole (0.98 g, 14.4 mmol), and DMF (10 mL) was stirred at room temperature overnight. Brine and hexane were added. The resulting mixture was stirred for 1 h and extracted with hexane three times. The combined organic layers were dried and concentrated to give silyl ester **22**, which was used for the next reaction without further purification. – A mixture of the silyl ester **22** and K_2CO_3 (1.00 g, 7.24 mmol) in MeOH (20 mL) was stirred at room temperature for 1 h and diluted with EtOAc. The resulting mixture was acidified slightly by addition of 1 N HCl and the product was extracted with EtOAc repeatedly. The combined organic layers were dried and concentrated to give an oily residue, which was purified by chromatography to furnish a mixture of acid (3'*R*)-**5** and TBSOH. The quantity of the products was calculated by using the ^1H NMR integration. (3'*R*)-**5** (1.33 g, 78% yield from iodolactone **20**) and TBSOH (125 mg). – (3'*R*)-**5**: ^1H NMR: δ = 0.07 and 0.10 (2 s, 6 H), 0.86 (s, 9 H), 2.49–2.61 (m, 2 H), 4.83 (q, J = 6 Hz, 1 H), 6.25–6.34 (m, 2 H). – This mixture was used for the next reaction without further purification.

Amide (5*S*,3'*R*)-6**:** To a solution of acid (3'*R*)-**5** (200 mg, 0.56 mmol, 99% *ee*), (5*S*)-**4** (76 mg, 0.54 mmol, 95% *ee*), DMAP (13 mg, 0.11 mmol), and PPTS (40 mg, 0.16 mmol) in CH_2Cl_2 (1 mL) was added a solution of DCC (130 mg, 0.63 mmol) in CH_2Cl_2 (0.7 mL). The resulting mixture was stirred at room temperature overnight and concentrated to leave an oil, which was purified by chromatography (hexane/EtOAc) to afford (5*S*,3'*R*)-**6** (209 mg, 82%). – $[\alpha]_{\text{D}}^{28}$ = -25 (c = 0.978, CHCl_3). – IR (neat): $\tilde{\nu}$ = 3319, 1751, 1693, 1655 cm^{-1} . – ^1H NMR: δ = 0.09 (s, 6 H), 0.85 (t, J = 7.5 Hz, 3 H), 0.87 (s, 9 H), 1.47 (s, 3 H), 1.7–1.9 (m, 2 H), 2.52 (dd, J = 14, 7 Hz, 1 H), 2.61 (dd, J = 14, 4 Hz, 1 H), 4.79 (dt, J = 4, 7 Hz, 1 H), 6.26–6.37 (m, 2 H), 7.34 (s, 1 H), 8.23 (br. s, 1 H). – ^{13}C NMR: δ = 169.3, 169.2, 142.2, 134.0, 124.8, 88.4, 82.1, 73.3, 43.7, 32.0, 25.7, 24.4, 17.9, 8.1, –4.5, –5.1. – $\text{C}_{18}\text{H}_{30}\text{INO}_4\text{Si}$ (479.4): calcd. C 45.09, H 6.31; found C 45.26, H 6.45.

Amide (5*S*,3'*S*)-6**:** According to the above procedure, the title compound was prepared from (5*S*)-**4** and (3'*S*)-**5** in 77% yield. – $[\alpha]_{\text{D}}^{27}$ = -1 (c = 1.02, CHCl_3). The ^1H and ^{13}C NMR spectra are superimposed with those of (5*S*,3'*R*)-**6**.

Ethyl (E)-2-Undecenoate: To an ice-cold suspension of NaH (3.10 g, 55% suspension in mineral oil, 71.0 mmol) in THF (100 mL) was added triethyl phosphonoacetate (21.5 g, 95.8 mmol) and the mixture was warmed up to room temperature over 30 min with stirring. 1-Nonanal (**28**) (8.30 g, 58.4 mmol) was added, and the mixture was stirred at room temperature for 10 min. Brine was added and the resulting mixture was extracted three times with Et_2O . The combined extracts were dried and concentrated to give an oily residue, which was purified by chromatography to afford ethyl (E)-2-undecenoate as an oil, the ^1H NMR spectrum of which is identical with those reported previously.^[22] The ^1H NMR and other spectroscopic data of the ester are updated. – IR (neat): $\tilde{\nu}$ = 1724, 1655 cm^{-1} . – ^1H NMR: δ = 0.86 (t, J = 7 Hz, 3 H), 1.18–1.38 (m, 13 H), 1.38–1.49 (m, 2 H), 2.17 (dq, J = 2, 7 Hz, 2 H), 4.17 (q, J = 7 Hz, 2 H), 5.79 (dt, J = 15, 2 Hz, 1 H), 6.95 (dt, J = 15, 7 Hz, 1 H). – ^{13}C NMR: δ = 167.0, 149.7, 121.4, 60.1, 32.2, 31.8, 29.3, 29.2, 29.1, 28.0, 22.6, 14.2, 14.0.

(E)-2-Undecen-1-ol (29): To a solution of the above ethyl ester, dissolved in THF (100 mL), DIBAL (154 mL, 0.95 M in toluene, 146 mmol) was added dropwise at -70°C . The mixture was stirred at -70°C for 1 h, and the solution was poured into a mixture of EtOAc and 1 N HCl at 0°C with vigorous stirring. The layers were separated and the aqueous layer was extracted with EtOAc three times. The combined organic layers were dried and concentrated to furnish an oily residue, which was purified by distillation to afford alcohol **29** (8.86 g) in 89% yield from **28**. The ^1H NMR spectrum of **29** is identical with the data reported.^[22] Other data of **29** are provided. – B.p. 150°C (5 Torr). – IR (neat): $\tilde{\nu}$ = 3325, 970 cm^{-1} . – ^{13}C NMR: δ = 133.8, 129.0, 63.9, 32.2, 31.9, 29.5, 29.3, 29.2, 29.1, 22.7, 14.1.

(E)-1-Chloro-2-undecene (30): A mixture of **29** (3.00 g, 17.6 mmol), PPh_3 (6.92 g, 26.4 mmol), and CCl_4 (9 mL) was stirred at room temperature for 4 d, diluted with hexane, and filtered through a pad of Celite with hexane. The filtrate was concentrated to give an oil, which was purified by chromatography (hexane) to afford **30** (2.68 g, 81%). – IR (neat): $\tilde{\nu}$ = 1250, 966 cm^{-1} . – ^1H NMR: δ = 0.88 (t, J = 7 Hz, 3 H), 1.20–1.44 (m, 12 H), 2.05 (q, J = 7 Hz, 2 H), 4.03 (dt, J = 7, 1 Hz, 2 H), 5.61 (dt, J = 15, 7 Hz, 1 H), 5.76 (dt, J = 15, 7 Hz, 1 H). – ^{13}C NMR: δ = 136.5, 126.0, 45.6, 32.1, 31.9, 29.4, 29.2, 29.1, 28.8, 22.7, 14.1. – $\text{C}_{11}\text{H}_{21}\text{Cl}$ (188.7): calcd. C 70.00, H 11.21; found C 70.28, H 11.34.

(2*R*,3*S*)-1-Chloroundecane-2,3-diol (31): To an ice-cold mixture of AD-mix- α (28 g) and MeSO₂NH₂ (1.90 g, 20.0 mmol) in *t*BuOH (100 mL) and H₂O (100 mL), **30** (3.78 g, 20.0 mmol) was added dropwise. The mixture was stirred at 0 °C for 24 h and the excess reagent was destroyed with NaHSO₃ (28 g, 270 mmol) at 0 °C for 30 min. The product was extracted with EtOAc twice. The combined extracts were washed with 2 N KOH to remove most of the MeSO₂NH₂. The mixture was then dried, and concentrated to furnish diol **31**, which was used for the next reaction without further purification. An enantiomeric excess of 90% was later determined at the stage of epoxy alcohol **32** (vide infra). Analytically pure **31** was obtained by chromatography. – IR (nujol): $\tilde{\nu}$ = 3367, 3275 cm⁻¹. – ¹H NMR: δ = 0.87 (t, *J* = 7 Hz, 3 H), 1.17–1.58 (m, 14 H), 2.4 (br. s, 1 H), 2.9 (br. s, 1 H), 3.54–3.72 (m, 4 H). – ¹³C NMR: δ = 73.8, 71.6, 46.8, 33.6, 31.8, 29.52, 29.49, 29.2, 25.5, 22.6, 14.0. – C₁₁H₂₃ClO₂ (222.8): calcd. C 59.31, H 10.41; found C 59.46, H 10.53.

(2*S*,3*S*)-1,2-Epoxyundecan-3-ol (32): To a solution of the above diol **31**, dissolved in THF (40 mL), was added crushed NaOH (3.93 g, 98.3 mmol). The mixture was stirred at room temperature for 30 min, and diluted with brine. The resulting mixture was extracted with EtOAc three times, and the combined extracts were dried and concentrated to afford a residue. Purification by chromatography (hexane/EtOAc) afforded **32** (3.17 g, 84% from chloride **30**), which was 90% *ee* by ¹H NMR spectroscopy of the derived MTPA ester. – **32**: IR (neat): $\tilde{\nu}$ = 3421 cm⁻¹. – ¹H NMR: δ = 0.85 (t, *J* = 7 Hz, 3 H), 1.16–1.62 (m, 14 H), 2.26 (t, *J* = 6 Hz, 1 H), 2.69 (dd, *J* = 5, 3 Hz, 1 H), 2.80 (dd, *J* = 5, 4 Hz, 1 H), 2.95 (ddd, *J* = 5.5, 4, 3 Hz, 1 H), 3.39 (quint, *J* = 5.5 Hz, 1 H). – ¹³C NMR: δ = 71.8, 55.5, 45.2, 34.3, 31.8, 29.6, 29.4, 29.2, 25.3, 22.6, 14.0. – C₁₁H₂₂O₂ (186.3): calcd. C 70.92, H 11.90; found C 70.75, H 12.13.

(4*S*,5*R*)-4,5-Epoxytridecan-1-yne (35): To an ice-cold solution of **32** (1.00 g, 5.37 mmol) and Et₃N (1.73 g, 17.1 mmol) in CH₂Cl₂ (14 mL), MsCl (918 mg, 8.01 mmol) was added dropwise. The mixture was stirred at 0 °C for 30 min, and diluted with EtOAc and saturated NaHCO₃. After separation of the organic layer, the aqueous layer was extracted three times with EtOAc. The combined organic layers were dried and concentrated to give mesylate **33**, which was used for the next reaction without further purification. – To a solution of trimethylsilylacetylene (1.01 g, 10.3 mmol) in THF (15 mL) was added *n*BuLi (4.0 mL, 2.03 M in hexane, 8.12 mmol) at –78 °C. The mixture was stirred at –78 °C for 30 min, then BF₃·OEt₂ (1.30 g, 9.13 mmol) was added and, after 10 min of stirring, a solution of **33** in THF (7.5 mL) was added. The mixture was stirred between –78 and –60 °C for 30 min and poured into saturated NH₄Cl. The product was extracted with EtOAc three times. The combined extracts were dried and concentrated to leave the acetylenic alcohol **34**, which was somewhat unstable and used immediately for the next reaction without further purification. – To the above acetylene **34** in MeOH (16 mL), K₂CO₃ (2.26 g, 16.1 mmol) was added in portions. The mixture was stirred at room temperature for 8 h and poured into saturated NH₄Cl with EtOAc. The resulting mixture was extracted three times with EtOAc, and the combined organic layers were dried and concentrated to give an oil, which was purified by chromatography (hexane/EtOAc) to afford epoxy acetylene **35** (724 mg, 69% from epoxy alcohol **32** of 90% *ee*). – $[\alpha]_D^{25}$ = +42 (*c* = 1.002, CHCl₃). – IR (neat): $\tilde{\nu}$ = 3313, 2120 cm⁻¹. – ¹H NMR: δ = 0.87 (t, *J* = 7 Hz, 3 H), 1.18–1.58 (m, 14 H), 2.04 (t, *J* = 3 Hz, 1 H), 2.27 (ddd, *J* = 17, 7, 3 Hz, 1 H), 2.58 (ddd, *J* = 17, 6, 3 Hz, 1 H), 2.96 (dt, *J* = 4, 6 Hz, 1 H), 3.14 (ddd, *J* = 7, 6, 4 Hz, 1 H). – ¹³C NMR: δ = 79.5, 70.4, 57.0, 54.8, 31.8, 29.5, 29.2, 27.5, 26.4, 22.6,

18.5, 14.1. – C₁₃H₂₂O (194.3): calcd. C 80.35, H 11.41; found C 80.02, H 11.42.

(1'*E*,4'*S*,5'*R*)-2-(4',5'-Epoxy-1'-tridecenyl)-5,5-dimethyl-1,3,2-dioxaborinane [(9'*S*,10'*R*)-7]: To an ice-cold solution of BH₃·SMe₂ (3.0 mL, 2.0 M in THF, 6.0 mmol) was added (–)- α -pinene (2.05 g, 15.0 mmol). After stirring at 0 °C for 1 h, a white precipitate was observed. The ice bath was removed and the mixture was stirred for an additional 2 h to ensure complete formation of (Ipc)₂BH. The mixture was cooled to –30 °C and acetylene **35** (928 mg, 4.78 mmol) was added. The resulting mixture was allowed to warm up to 0 °C over 2 h with stirring to complete the hydroboration. To this solution acetaldehyde (3.31 g, 75.1 mmol) was added and the solution was heated under gentle reflux (bath temperature ca. 40 °C) overnight. The volatile compounds were removed in vacuo to leave **36** as a viscous oil, which was used for the next reaction without further purification. – A solution of **36** and 2,2-dimethyl-1,3-propanediol (575 mg, 5.52 mmol) in THF (10 mL) was stirred at room temperature for 3 h, and concentrated to furnish a mixture of the desired product and Ipc-OH, from which Ipc-OH was removed by bulb-to-bulb distillation [100–110 °C (1 Torr), 1–2 h]. Finally, the residue was purified by chromatography (hexane/EtOAc) to afford (9'*S*,10'*R*)-**7** (940 mg, 64%). – $[\alpha]_D^{26}$ = +21 (*c* = 0.928, CHCl₃). – IR (neat): $\tilde{\nu}$ = 1639, 1090, 999 cm⁻¹. – ¹H NMR: δ = 0.87 (t, *J* = 7 Hz, 3 H), 0.96 (s, 6 H), 1.20–1.58 (m, 14 H), 2.26 (ddt, *J* = 15, 1.5, 6 Hz, 1 H), 2.45 (ddt, *J* = 15, 1.5, 6 Hz, 1 H), 2.89–2.97 (m, 1 H), 3.02 (dt, *J* = 4, 6 Hz, 1 H), 3.63 (s, 4 H), 5.49 (dt, *J* = 18, 1.5 Hz, 1 H), 6.55 (dt, *J* = 18, 6 Hz, 1 H). – C₁₈H₃₃BO₃ (308.3): calcd. C 70.13, H 10.79; found C 69.88, H 10.60.

(1'*E*,4'*R*,5'*S*)-2-(4',5'-Epoxy-1'-tridecenyl)-5,5-dimethyl-1,3,2-dioxaborinane [(9'*R*,10'*S*)-7]: According to the procedure described above, the title compound ($[\alpha]_D^{26}$ = –23 (*c* = 1.03, CHCl₃)) was prepared from *ent*-**35** of > 99% *ee* ($[\alpha]_D^{29}$ = –46 (*c* = 0.982, CHCl₃)).

TBS Ether of (5*S*,3'*R*,9'*S*,10'*R*)-Korormicin (1) [(5*S*,3'*R*,9'*S*,10'*R*)-9]: To an ice-cold mixture of (9'*S*,10'*R*)-**7** (97 mg, 0.31 mmol, 90% *ee*), NiCl₂(dppf) (22 mg, 0.032 mmol), and THF (0.2 mL), MeLi (0.24 mL, 1.58 M in Et₂O, 0.38 mmol) was added. The resulting dark red solution was stirred at 0 °C for 15 min to generate the corresponding borate **8** and an active Ni⁰ species. To this solution was added (5*S*,3'*R*)-**6** (100 mg, 0.21 mmol, 94% *ds*) at 0 °C. The cooling bath was removed and the mixture was stirred at room temperature for 4 h. Saturated NH₄Cl was added, and the resulting mixture was extracted with Et₂O three times. The combined organic layers were dried and concentrated to furnish a brown residue, which was purified by chromatography to afford (5*S*,3'*R*,9'*S*,10'*R*)-**9** (56 mg, 49%) as a viscous oil. – IR (neat): $\tilde{\nu}$ = 3321, 1765, 1701, 1655, 837, 779 cm⁻¹. – ¹H NMR: δ = 0.04 (s, 3 H), 0.05 (s, 3 H), 0.8–0.9 (m, 15 H), 1.47 (s, 3 H), 1.1–1.6 (m, 12 H), 1.70–1.88 (m, 2 H), 2.24–2.59 (m, 4 H), 2.92–3.00 (m, 2 H), 4.95–5.04 (m, 1 H), 5.35 (dd, *J* = 11, 8 Hz, 1 H), 5.78 (dt, *J* = 15, 7 Hz, 1 H), 5.97 (t, *J* = 11 Hz, 1 H), 6.39 (dd, *J* = 15, 11 Hz, 1 H), 7.33 (s, 1 H), 8.15 (br. s, 1 H). – ¹³C NMR: δ = 169.9, 169.3, 133.8, 132.3, 131.3, 129.0, 126.9, 124.9, 88.3, 66.6, 57.1, 55.9, 45.9, 32.0, 31.8, 31.5, 29.51, 29.50, 29.2, 27.7, 26.6, 25.7, 24.4, 22.6, 18.0, 14.1, 8.1, –4.4, –5.2. – C₃₁H₅₃NO₅Si (547.8): calcd. C 67.96, H 9.75; found C 67.77, H 9.44.

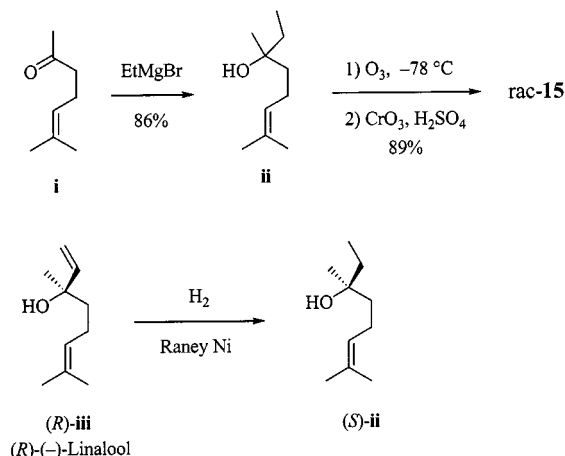
(5*S*,3'*R*,9'*S*,10'*R*)-Korormicin (1) (Natural Type): To the silyl ether **9** (100 mg, 0.18 mmol), dissolved in THF (1 mL), Bu₄NF (0.36 mL, 1.0 M in THF, 0.36 mmol) was added dropwise. The solution was stirred at room temperature for 1 h and poured into buffer (pH = 5) and Et₂O with vigorous stirring. The organic layer was separated

and the aqueous layer was extracted with Et₂O twice. The combined organic layers were dried and concentrated to afford an oily residue, which was purified by chromatography to afford (5*S*,3'*R*,9'*S*,10'*R*)-**1** (67 mg, 86%). – [α]_D²⁰ = –24.5 (*c* = 0.828, EtOH) {ref.^[1a] [α]_D²⁵ = –24.4 (*c* = 0.29, EtOH)}. – The ¹H and ¹³C NMR spectra of synthetic **1** in [D₆]DMSO are identical with those reported.^[1a] The following spectroscopic data were obtained in CDCl₃. – ¹H NMR: δ = 0.86 (t, *J* = 7 Hz, 3 H), 0.88 (t, *J* = 7 Hz, 3 H), 1.47 (s, 3 H), 1.1–1.6 (m, 12 H), 1.68–1.92 (m, 2 H), 2.28–2.41 (m, 2 H), 2.57 (dd, *J* = 16, 3.5 Hz, 1 H), 2.62 (dd, *J* = 16, 8 Hz, 1 H), 2.91–3.01 (m, 2 H), 3.08 (br. s, 1 H), 4.98–5.08 (m, 1 H), 5.39 (dd, *J* = 11, 9 Hz, 1 H), 5.81 (dt, *J* = 15, 7 Hz, 1 H), 6.06 (t, *J* = 11 Hz, 1 H), 6.45 (dd, *J* = 15, 11 Hz, 1 H), 7.36 (s, 1 H), 8.46 (br. s, 1 H). – ¹³C NMR: δ = 170.7, 169.5, 134.4, 132.8, 130.9, 129.9, 127.0, 124.8, 88.6, 64.7, 57.2, 55.9, 43.4, 32.0, 31.8, 31.4, 29.5, 29.2, 27.7, 26.5, 24.2, 22.6, 14.0, 8.2.

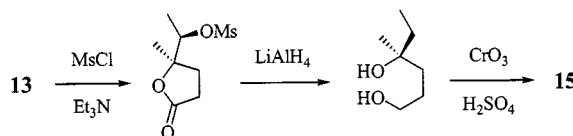
Acknowledgments

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Government of Japan.

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- of (*R*)-**iii** is reported by Vlad.^[8b] However, it was later found that (*R*)-**iii** is not available even though both the enantiomers of **iii** are found in the Merck Index.^[8c] Major companies including Merck now produce it as a racemic form. – [8b] P. Vlad, M. Soucek, *Coll. Czech. Chem. Commun.* **1962**, *27*, 1726–1729. – [8c] *The Merck Index*, 12th ed. (Ed.: S. Budavari), Merck & Co., Inc., Whitehouse Station, NJ, **1996**, 5520 Linalool.
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Received November 10, 2000
 [O00569]