Enantioselective Total Synthesis of *cis*-Trikentrin B

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Natural *cis*-trikentrin B was synthesized enantioselectively using, as key steps, an intramolecular Diels−Alder reaction of an allenic dienamide followed by aromatization to construct an indole ring and cleavage of bicyclo[2.2.1]heptene to launch a *cis*-dimethylcyclopentane ring. Diels−Alder adducts **9** and **10** were elaborated to provide allenic dienamide **25**, and its intramolecular Diels−Alder reaction proceeded smoothly. Aromatization to an indole ring and stereoselective cleavage of the bicyclo[2.2.1]heptene ring were performed successfully. Introduction of an (*E*)-butenyl group *via* addition of propylmagnesium bromide and subsequent anti elimination of water gave natural *cis*-trikentrin B.

Introduction

Trikentrins are a series of polyalkylindole alkaloids that were isolated from the marine sponge *Trikentrion flabelliforme* collected from coastal waters off Darwin, Australia, by Capon *et al.* in 1986 (Figure 1).[1]

The structures and relative configurations of these compounds were also reported by Capon's group. This series of alkaloids exhibits growth inhibitory activity toward the Gram-positive bacteria *Bacillus subtilis*.[1] This is a new class of indole alkaloid in that, in addition to having an alkyl substituent, these compounds contain a dimethylcyclopentane ring fused to the benzene ring of the indole skeleton. Because of their unique structure and lack of structural relationship with major antibiotics, trikentrins have intrigued many chemists.

cis-Trikentrin B (**1**) is a minor component in the isolate, occupying 0.007% of the dry weight, and is obtained only as a mixture with *trans*-isotrikentrin B (**2**).[1] Several syntheses have been reported in this family, not only to develop synthetic routes, but also to establish the absolute configuration of the *cis* and *trans* trikentrins.

The first total synthesis of trikentrin A was culminated by MacLeod *et al.* using aryl radical cyclization as the main strategy.[2a] Later, Boger *et al.* reported synthesis based on a heteroaromatic azadiene Diels−Alder reaction.[2b]

The first total synthesis of *cis*-trikentrin B was reported by our laboratory, using our new strategy to construct the indole skeleton by an intramolecular Diels−Alder reaction of allenic dienamide.[2c] During the course of our systematic studies, Natsume *et al.* reported the first asymmetric synthesis of *cis*-trikentrin B and assigned the absolute configuration as 6*R*,8*S* through comparison of CD spectra of the mixture of synthesized *cis*-trikentrin B and *trans*-trikentrin B with that of an authentic sample.[2d] Herein, we report the full details of an asymmetric synthesis using the strategy that we developed in the racemic total synthesis of *cis*-trikentrin B (eq 1).[2c]

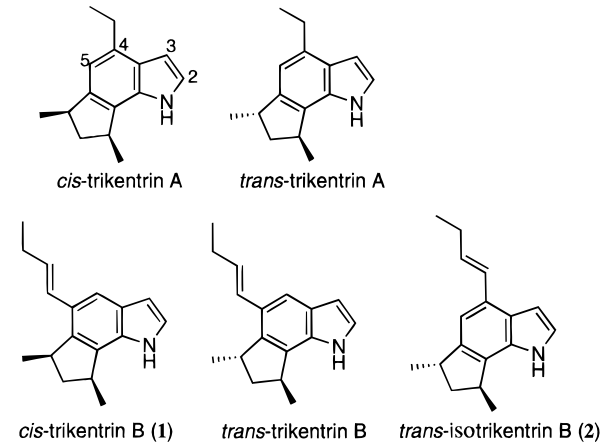
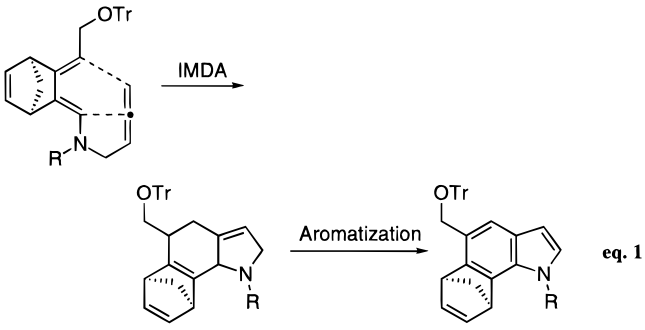


Figure 1. Trikentrins.



eq. 1

Basic strategy for constructing the indole skeleton

The strategy is based on the facile formation of a partially hydrogenated indole skeleton *via* an intramolecular Diels−Alder reaction, exploiting the high reactivity of allene as a dienophile. The merit of this strategy in constructing polyalkylindole skeletons like the trikentrins lies in the potential to control the site of substitution through modification of the substitution pattern on the allenic dienamide. As seen in eq 1, a substituent on the terminal carbon of the diene portion can be converted to a substituent on C5 directly.

The second point of this strategy is concerned with stereoselective cleavage of the bicyclo[2.2.1]heptene system derived from the Diels−Alder adduct of cyclopentadiene to lead to the *cis*-disubstituted cyclopentane ring, followed by a series of transformations that result in *cis*-dimethyl groups. Our retrosynthetic analysis is outlined in Scheme 1.

[⊗] Abstract published in *Advance ACS Abstracts,* May 1, 1996.

(1) (a) Capon, R. J.; MacLeod, J. K.; Scammells, P. J. *Tetrahedron* **1986**, *42*, 6545. (b) Herb, R.; Carroll, A. R.; Yoshida, W. Y.; Scheuer, P. J.; Paul, V. J. *Tetrahedron* **1990**, *46*, 3089.

(2) (a) MacLeod, J. K.; Monahan, L. C. *Tetrahedron Lett.* **1988**, *29*, 391. (b) Boger, D. L.; Zhang, M. *J. Am. Chem. Soc.* **1991**, *113*, 4230. (c) Yasukouchi, T.; Kanematsu, K. *Tetrahedron Lett.* **1989**, *30*, 6559. (d) Muratake, H.; Mikawa, A.; Seino, T.; Natsume, M. *Chem. Pharm. Bull.* **1994**, *42*, 846.

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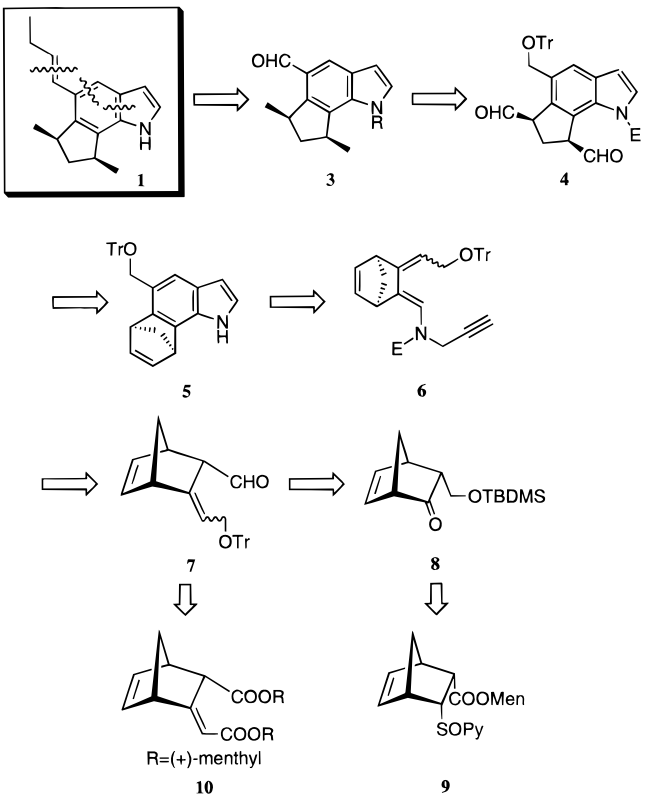
Scheme 1. Retrosynthetic Analysis



1 3 4 5 6 7 8 10 9

In constructing the *cis*-dimethylcyclopentane ring enantioselectively, the enantiomeric purity depends exclusively on the facial selectivity and regioselectivity of the intermolecular Diels−Alder reaction to prepare the bicyclo[2.2.1]heptene ring. If we can prepare a stereocontrolled Diels−Alder adduct as a synthon, after indole ring formation, the facial selectivity can be converted to enantioselectivity during the cleavage of the double bond of the bicyclo[2.2.1]heptene system.

We chose Koizumi's sulfoxide **9**[3] as the starting material. Using proper transformations, it was envisaged that sulfoxide **9** would be converted to ketosilyl ether **8** easily. The carbonyl group was destined to be converted to an exocyclic olefin and part of a diene. Compound **8**, which was employed in our racemic synthesis,[2c] could lead to **7**. Oppolzer's two-step conversion proved to be a convenient method of generating dienes like **6** in the racemic synthesis.[2c,4] However, later, we developed a new synthon **10** using our original strategy that employs allene-1,3-dicarboxylate as a dienophile.[5] So, the conversion of **10** to **7** was also investigated for applicability. Homologative allenylation can give the key intermediate, allenic dienamide.[6]

After the construction of indole **5**, it appeared to be clear that the cleavage of the bicyclo[2.2.1]heptene ring would lead to the *cis*-disubstituted cyclopentane ring of compound **4**. The manipulation of the substituents to the dimethyl groups of compound **3** would be executed under mild conditions to prevent epimerization.

The last problem that remained was the introduction of an (*E*)-butenyl group at the C6 position of the indole ring. We employed a Wittig reaction in our previously reported study which resulted in a *Z*, *E* mixture from which the *E* isomer was difficult to isolate.

In the present synthesis, we adopted Natsume's method of addition−anti elimination used in his synthesis of *cis*-trikentrin B.[2d]

Results and Discussion

Koizumi's Diels−Alder adduct was prepared according to his report[3] (Scheme 2). A diastereomeric mixture of sulfoxides **13** and **14** was isolated by fractional crystallization using hexane−diethyl ether as the solvent.

During the early stages of our investigation, this operation was performed by the common method of preferential crystallization of one diastereomer.[7] But this was time-consuming and limited to a small scale operation. Eventually, by careful regulation of the crystallization conditions, the two diastereomers were crystallized in morphologically different crystals discernible with the naked eye (cubics of about 1 cm diameter and needles of 3 mm width and over 2 cm length), and the isolation was performed by simply picking out the different crystals with tweezers.

The *R* diastereomer **14** was used in the synthesis, and the *S* diastereomer **13** was epimerized to afford an *R*,*S* mixture using a reduction−reoxidation process. Initially, this process was performed with two sequential reactions using titanium trichloride followed by *m*-chloroperbenzoic acid. Over the series of steps, *Z*−*E* isomerization occurred, and the *Z*:*E* ratio obtained was similar to that observed during the original conversion of **11** to **12**. Later, a more convenient method of oxidoreduction, using both titanium trichloride and hydrogen peroxide in one pot, was developed, combining the two reactions.[8] Addition of titanium trichloride to an ethanolic solution of sulfide at room temperature until the violet color of the reagent no longer disappeared and consecutive addition of hydrogen peroxide gave good results.

However, the problem of *Z*−*E* isomerization persisted. Oxidation of the sulfide with *m*-chloroperbenzoic acid gave sulfoxide in the same *Z*:*E* ratio as that of the reaction with hydrogen peroxide. A pH-controlled oxidation with monoperoxyphthalic acid magnesium salt (MMPP) in a buffered solution (pH 7.0) gave the same result. These facts suggested that *Z*−*E* isomerization occurs in the reduction stage with titanium trichloride.

The Diels−Alder reaction, according to Koizumi's method, afforded the adduct in excellent yield with good enantioselectivity.[3b] The obtained Diels−Alder adduct was transformed as shown in Scheme 3.

The adduct **9** was taken to **15** *via* a Pummerer rearrangement and then transformed to dimethylketalized compound **16** for further reaction.

We originally planned to prepare compound **20** to fix the *endo* configuration of the menthyl ester moiety so as to simplify subsequent operations, but the elimination of trifluoroacetic acid occurred spontaneously under the reaction conditions. Fortunately, the *endo* configuration of the menthyl ester was revived in the ketalization step to make the operations and spectral analyses of the

(3) (a) Takayama, H.; Iyobe, A.; Koizumi, T. *Chem. Commun.* **1986**, 771. (b) Arai, Y.; Hayashi, Y.; Yamamoto, M.; Takayama, H.; Koizumi T. *Chem. Lett.* **1987**, 185.

(4) (a) Oppolzer, W.; Bieber, L.; Francotte, E. *Tetrahedron Lett.* **1979**, *11*, 981. (b) Kiefer, H. *Synthesis* **1972**, 39.

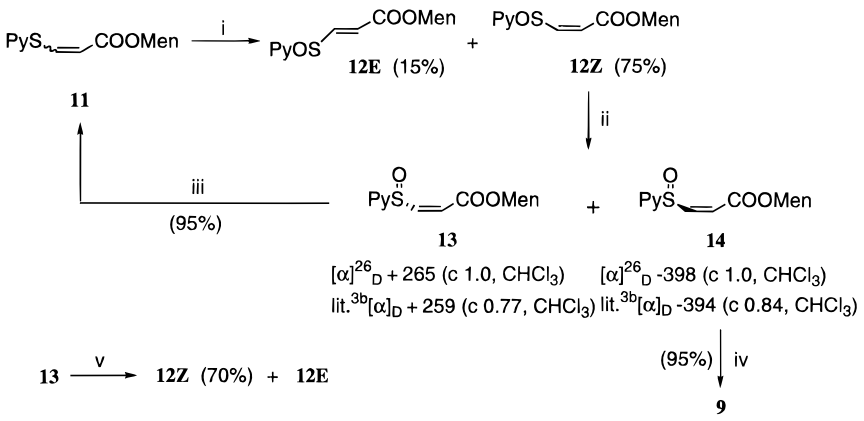
(5) Aso, M.; Ikeda, I.; Kawabe, T.; Shiro, M.; Kanematsu, K. *Tetrahedron Lett.* **1992**, *33*, 5787.

(6) Crabbe, P.; Fillion H.; Andre, D.; Luche J.-L. *Chem. Commun.* **1979**, 859.

(7) Jacques, J.; Collet, A.; Wilen, S. H. *Enantiomers, Racemates and Resolutions*; John Wiley & Sons: New York, 1981.

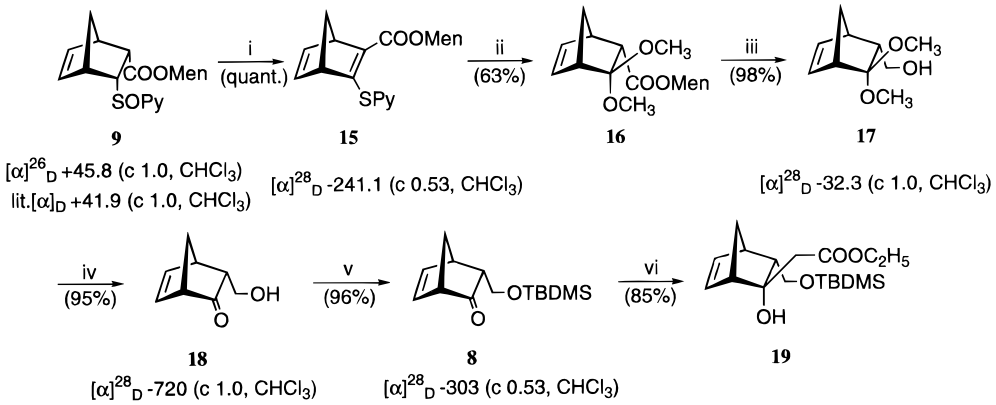
(8) (a) Takayama, H.; Hayashi, K.; Koizumi, T. *Tetrahedron Lett.* **1986**, *27*, 5509. (b) Watanabe, Y.; Numata, T.; Oae, S. *Synthesis* **1981**, 204.

Scheme 2[a]



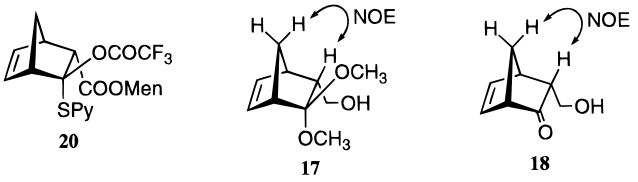
[a] Reagents and conditions: (i) *m*-CPBA, CH_2Cl_2, 0 °C; chromatographed; (ii) fractional crystallization; (iii) $TiCl_3$, EtOH, rt; (iv) Et_2AlCl in hexane, cyclopentadiene, CH_2Cl_2, −78 °C; (v) $TiCl_3$, EtOH, rt; then H_2O_2, 0 °C.

Scheme 3[a]



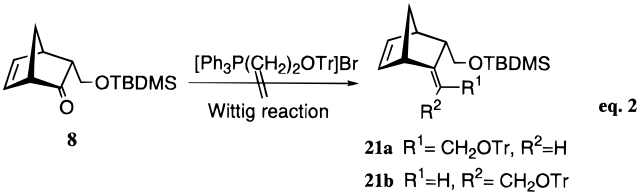
[a] Reagents and conditions: (i) TFAA, 2,6-lutidine, CH_2Cl_2, rt; (ii) methyl orthoformate, MeOH, *p*-TsOH, reflux; (iii) $LiAlH_4$, ether, rt; (iv) 5% HCl, THF; (v) TBDMSCl, imidazole, DMAP, CH_2Cl_2, rt; (vi) Reformatsky reaction.

following steps simple. This fact was confirmed by NOESY spectra of compounds **17** and **18**.



Reduction with lithium aluminum hydride and subsequent deketalization gave keto alcohol **18** in good yield. Next, the alcohol was protected with a *tert*-butyldimethylsilyl group.

Direct transformation of compound **8** to compound **21** by a Wittig reaction did not occur under various conditions probably because of the bulkiness of both reactants and the lability of **8** in considerably basic conditions (eq 2).



eq. 2

This difficulty was circumvented by an addition−dehydration method. A classical Reformatsky reaction proceeded in refluxing dry tetrahydrofuran.[9a] However, the yield was low and unreproducible. A modified reaction using silver-doped zinc laminate could not be controlled easily.[9b] The reaction hardly occurred under −10 °C and gave decomposed products above 0 °C. Mukaiyama's method, which employs metallic zinc generated *in situ*, proceeded smoothly at room temperature to a certain point but no further and resulted in a modest yield even with a large excess of reagents.[9c]

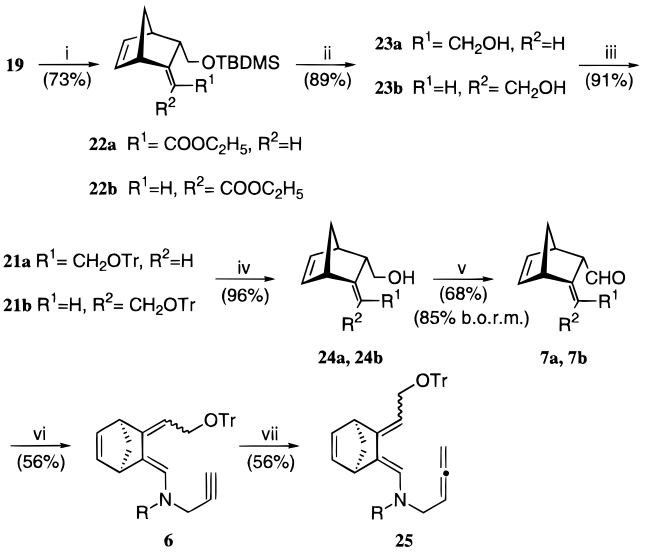
Finally, Toda's Reformatsky reaction in the absence of solvent was adopted.[9d] This reaction proceeded at room temperature in good yield and, moreover, cleanly, making it possible to recover the unreacted starting material easily. This reaction occurred stereoselectively and afforded compound **19** *via* attack from the convex face.

Next, transformation to launch diene and dienophile was attempted (Scheme 4).

Dehydration of **19** was accomplished under basic conditions with thionyl chloride and triethylamine. This anti elimination step afforded *Z*,*E* geometric isomers in almost equal amounts. After the cyclization and aromatization, these two isomers should give the same product, so the unseparated mixture was carried on. However, for the purpose of comparison with the regioconfirmed

(9) (a) For a review, see: Fürstner, A. *Synthesis* **1989**, 571. (b) Csuk, R.; Fürstner, A.; Weidmann, H. *Chem. Commun.* **1986**, 775. (c) Harada, T.; Mukaiyama, T. *Chem. Lett.* **1982**, 161. (d) Tanaka, K.; Kishigami, S.; Toda, F. *J. Org. Chem.* **1991**, *56*, 4333.

Scheme 4[a]



[a] Reagents and conditions: (i) thionyl chloride, pyridine, 0 °C; (ii) DIBALH, ether, 0 °C; (iii) TrCl, TEA, DMAP, CH_2Cl_2, rt; (iv) Bu_4NF in THF solution, rt; (v) PCC, Celite, CH_2Cl_2, rt; (vi) propargylamine, MS 4A, ether; pivaloyl chloride, 2,4,6-collidine, CH_2Cl_2, rt; (vii) formalin diisopropylamine, CuBr, 1,4-dioxane, reflux.

synthesis to be described in Scheme 5, isolation on a spectroscopic scale was performed at each step.

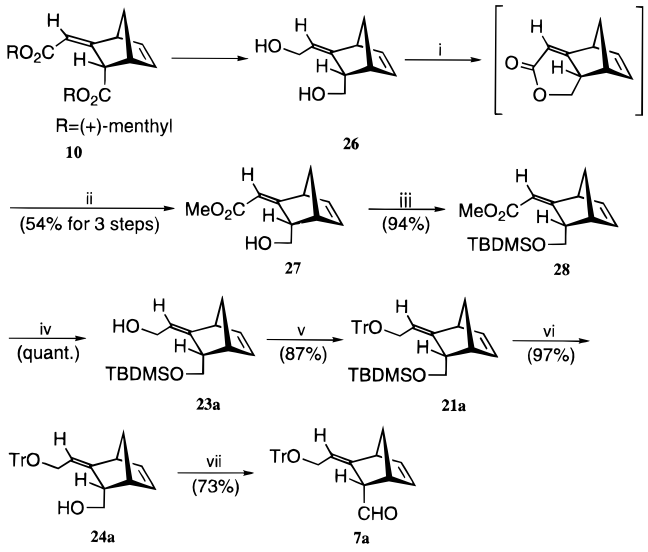
Reduction with diisobutylaluminum hydride afforded compound **23**, which was transformed to trityl ether **21**. Deprotection of silyl ether **21** followed by oxidation with pyridinium chlorochromate on celite afforded aldehyde **7**.[10] This oxidation step proceeded at a fast rate for 2 h and then slowed. This was not prevented by a large excess of reagent, probably because of the formation of acetal between the starting material and the product aldehyde **7**, given the acidic nature of pyridinium chlorochromate. However, a buffered reaction using sodium acetate powder resulted in a slower reaction. Reaction with neutral pyridinium dichromate proceeded very slowly as well. Thus, the starting material was recycled after 2 h of reaction and subsequent isolation from product.

Reaction of **7** with propargylamine in the presence of molecular sieves gave the desired propargylimine compound, and according to Oppolzer's method, this was immediately treated with pivaloyl chloride using collidine as a base.[4a] The resulting propargylamine compound **6** was treated with formaldehyde and diisopropylamine and a catalytic amount of cuprous bromide according to the Crabbe protocol of homologative allenylation.[6]

Later, we developed a more convenient synthon for preparing the key intermediate **7**.[5] This synthon **10** was prepared by Diels–Alder reaction of cyclopentadiene with optically active allene-1,3-dicarboxylate. The absolute configuration of this compound had been confirmed by X-ray analysis, and the applicability of this synthon had been proved by its successful conversion to cyclosarkomycin.[11]

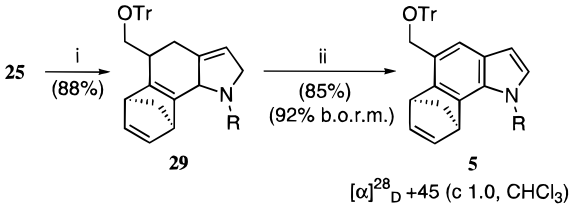
Compound **10** was converted to **26** according to the cyclosarkomycin synthesis,[11] and **26** was oxidized following Fetizon's procedure.[12] The lactone thus produced was

Scheme 5[a]



[a] Reagents and conditions: (i) Ag_2CO_3 on Celite, benzene, reflux; (ii) LiOH, THF–H_2O; $TMSCHN_2$, MeOH–benzene; (iii) TBDMSCl, imidazole, DMAP, CH_2Cl_2; (iv) DIBALH, CH_2Cl_2, −78 °C; (v) TrCl, TEA, DMAP, CH_2Cl_2; (vi) Bu_4NF in THF (vii) PCC, CH_2Cl_2.

Scheme 6[a]



[a] Reagents and conditions: (i) toluene, 160 °C, sealed tube; (ii) MnO_2, CH_2Cl_2, rt.

hydrolyzed and esterified with Shioiri's reagent[13] without purification (Scheme 5). The procedures outlined in Scheme 4 then afforded synthetic intermediate **7** in good yield.

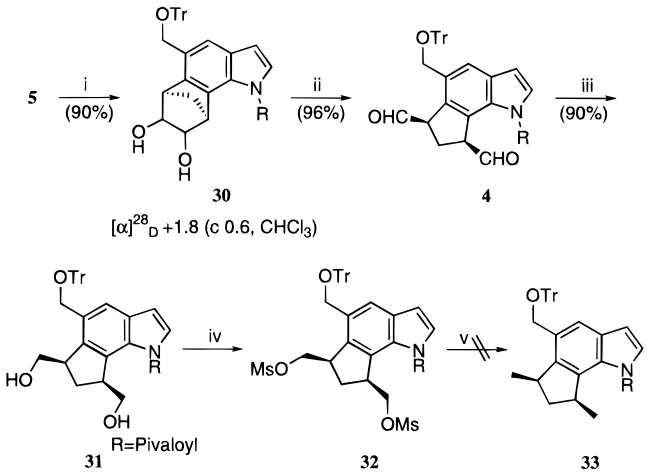
The spectra of the intermediates shown in Scheme 5 were compared with those of the intermediates shown in Scheme 4. The less polar compound **22a** showed spectral patterns similar to the corresponding methyl ester **28**, and the structure of the more polar compound was assigned as regioisomeric structure **22b**. The spectroscopic data of **23a** and successive compounds all matched.

Intramolecular Diels–Alder reaction of the allenic dienamide **25** in a sealed tube proceeded smoothly to give cyclized compound in 88% yield (Scheme 6).

Previous reports from our laboratory on the effects of substituents stated that a substituent on the same position of the diene as the (trityloxy)methyl group of compound **25** retards the intramolecular Diels–Alder reaction.[14a] But, the problem of the contribution of the *s-cis* conformer can be precluded by adopting the exocyclic diene fixed in a rigid ring system. The steric hindrance of the bulky (trityloxy)methyl group can be compensated for by the effect of a pivaloyl group, bringing the diene

(10) For a review, see: Piancatelli, G.; Scettri, A.; D'awia, M. *Synthesis* **1982**, 245.
(11) Ikeda, I.; Kanematsu, K. *Chem. Commun.* **1995**, 453.
(12) (a) Balogh, V.; Fetizon, M.; Golfier, M. *J. Org. Chem.* **1971**, *36*, 1339. (b) McKillop, A.; Young, D. W. *Synthesis* **1979**, 401.
(13) (a) Shioiri, T.; Aoyama, T. *Yuki Gosei Kagaku Kyokai Shi* **1986**, *44*, 149. (b) Hashimoto, N.; Aoyama, T.; Shioiri, T. *Chem. Pharm. Bull.* **1981**, *29*, 1475. (c) Mori, S.; Sakai, I.; Aoyama, T.; Shioiri, T. *Ibid.* **1982**, *30*, 3380.

Scheme 7[a]



[a] Reagents and conditions: (i) OsO_4, $MsNH_2$, NMO, pyridine, ether−1,4-dioxane−H_2O, rt; (ii) $NaIO_4$, THF−H_2O, rt; (iii) $NaBH_4$ (0.25 equiv), EtOH, −10 °C; (iv) MsCl, TEA, ether, 0 °C; (v) Zn, NaI, DME, reflux.

and the allenic dienophile moieties in closer proximity to facilitate the reaction.[14]

Aromatization of the obtained cyclic product represents another important point of our strategy. Using *p*-chloranil in refluxing tetrahydrofuran produced irreproducible results and often resulted in yields below 10%. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) or *o*-chloranil did not afford the desired product. In the end, aromatization with manganese dioxide proceeded at room temperature, and the recovery of the remaining starting material was easy.[15]

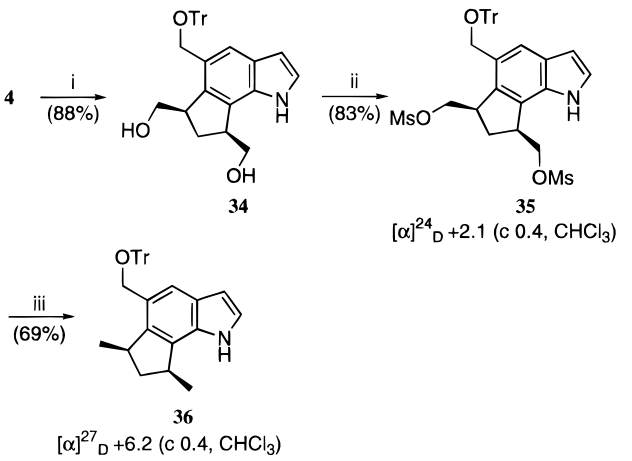
The stereoselective cleavage of the bicyclo[2.2.1]-heptene ring and installation of the *cis*-dimethyl groups commenced with dihydroxylation of the olefin using a catalytic amount of osmium tetraoxide with *N*-methylmorpholine *N*-oxide as a cooxidant and a stoichiomeric amount of methanesulfonamide[16] (Scheme 7).

The reaction proceeded at the same speed when using *p*-toluenesulfonamide; however, methanesulfonamide was adopted for practical reasons in that the R_f value of the product **30** was near that of *p*-toluenesulfonamide.

Further oxidation of the diol with sodium periodate gave *cis*-dialdehyde **4** in 96% yield. Direct cleavage using Lemieux oxidation conditions resulted in a low yield as in the reported case of simple bicyclo[2.2.1]heptene ring without the indole system.[2d,17] The selective reduction of aldehyde **4** containing the indolylamide moiety was effected by reduction with an exactly stoichiometric amount of sodium borohydride at −10 °C to give **31** in 90% yield.

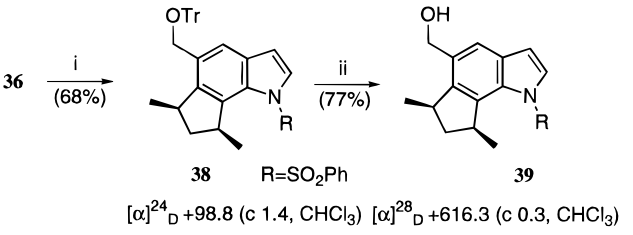
However, the subsequent mesylation afforded mainly monomesylated compounds in the presence of some desired dimesylate **32**. Moreover, the obtained dimesylate resisted to subsequent reduction to dimethyl compound **33**. Thus, we returned to compound **4**, and the reduction was conducted with an excess of sodium borohydride at room temperature to give wholly reduced compound **34** (Scheme 8).

Scheme 8[a]



[a] Reagents and conditions: (i) $NaBH_4$, MeOH, rt; (ii) MsCl, TEA ether, 0 °C; (iii) Zn, NaI, DME, reflux.

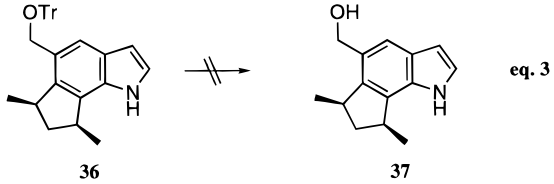
Scheme 9[a]



[a] Reagents and conditions: (i) $PhSO_2Cl$, NaH, 18-crown-6, THF, rt; (iii) CSA, MeOH−THF, rt.

The mesylation step proceeded cleanly under mild conditions, leaving no monomesylated product. Reduction of the dimesylate to dimethyl compound **36** was effected by Fujimoto's method.[18] Reduction of the same compound with Super hydride afforded many undesirable compounds probably because of the high basicity of the reagent along with its nucleophilicity.

Deprotection of the trityl ether with acid resulted in complete decomposition and loss of the indole skeleton (eq 3).



eq. 3

This was thought to be caused by the π excessive nature of the bare indole system which could induce electrophilic reaction of the ring system with acid. Accordingly, introduction of an electron-withdrawing group on the indole ring became necessary before treatment with acid (Scheme 9).

Introduction of a phenylsulfonyl group onto the nitrogen atom of the indole ring without producing the usually predominant 3-substituted isomer was accomplished with benzenesulfonyl chloride and sodium hydride using 18-crown-6 as a counterion to the indolyl anion, although

(14) (a) Hayakawa, K.; Yasukouchi, T.; Kanematsu, K. *Tetrahedron Lett.* **1986**, *27*, 1837. (b) Boeckman, Jr., R. K.; Ko, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1033. (c) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1991**, *113*, 224.

(15) Jansen, A. B. A.; Johnson,J. M.; Surtees, J. R. *J. Chem. Soc.* **1964**, 5573.

(16) Sharpless, K. B.; Amberg, W.; Bennani, Y.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768.

(17) Demuth, M.; Ritterskamp, P.; Weigt, E.; Schaffner, K. *J. Am. Chem. Soc.* **1986**, *108*, 4149.

(18) Fujimoto, Y.; Tatsuno, T. *Tetrahedron Lett.* **1976**, 3325.

in modest yield.[19] At first, this introduction was attempted with sodium hydride in refluxing dimethoxyethane solution and little compound **39** was obtained, while **38** was not obtained at all. Compound **38** obtained under the milder conditions described above proved to be unstable under the refluxing conditions used to synthesize it without crown ether.

Subsequent removal of the trityl group with acid proceeded smoothly at room temperature to give **39** in good yield, which is the same key intermediate Natsume *et al.* used in their synthesis of *cis*-trikentrin B. Spectral data agreed with those reported by Natsume.[2d]

Though the phenylsulfonyl group proved to be stable to Grignard reaction conditions and dehydration conditions with acid in Natsume's synthesis, it was difficult to introduce effectively because of the low activity of both the indole nitrogen as a nucleophile and benzenesulfonyl chloride as an electrophile. Given the low yield, we attempted to introduce a different electron-withdrawing protective group. This protective group should be introduced efficiently and should survive under Grignard conditions and the acidic conditions used in dehydration step.

First, we attempted to use a pivaloyl group, anticipating that this bulky group would prevent the indolyl amide from being deprotected by propylmagnesium bromide. However, it proved difficult to introduce this bulky group effectively.

We investigated the acetyl group which could be introduced in good yield and determined proper conditions for the Grignard reaction that avoided deprotection of the indolyl acetamide (Scheme 10).

The reaction of compound **36** with acetyl chloride and sodium hydride using 18-crown-6 afforded product **40** in 92% yield. Interestingly, the reaction using 15-crown-5 instead of 18-crown-6 did not proceed under the same conditions. However, 18-crown-6 and potassium *tert*-butoxide afforded **40** in a similar yield under the same conditions.[15]

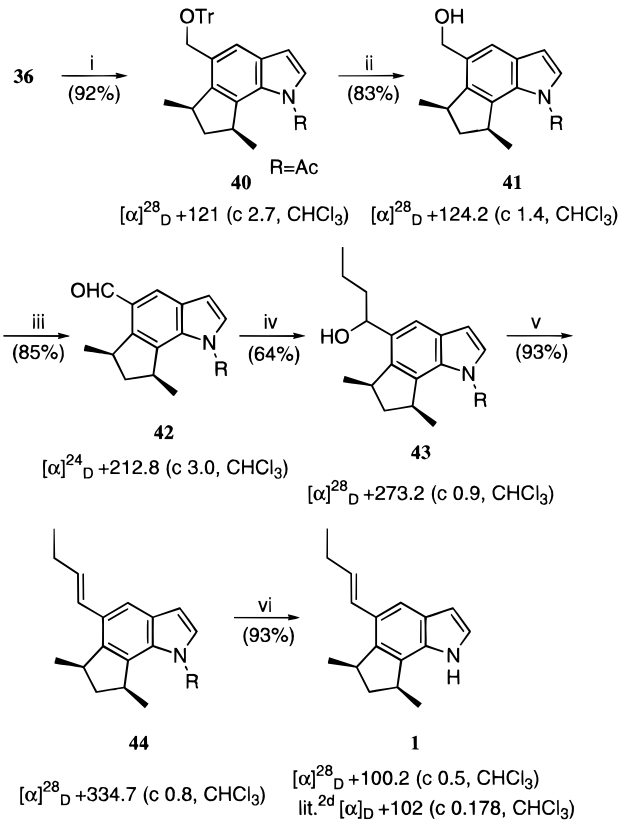
Subsequent deprotection of trityl ether and the oxidation of the thus obtained alcohol **41** was effected at room temperature. The addition of propylmagnesium bromide to aldehyde **42** conducted at −10 °C afforded compound **43** successfully without nucleophilic attack on the indolyl acetamide. Dehydration with *p*-toluenesulfonic acid completed the introduction of the 1 (*E*)-butenyl group.[2d]

Natsume *et al.* utilized refluxing ethanolic potassium hydroxide to remove the phenylsulfonyl group.[2d] Removal of the acetyl group from the nitrogen atom was effected by reduction with sodium borohydride at room temperature to give *cis*-trikentrin B, which is unstable and darkened on standing as in Capon's report.[1] IR, ^{1}H NMR, ^{13}C NMR, mass, and CD spectral data of **1** all agreed with those of Natsume (Figure 2).[2d]

Experimental Section

Melting points were uncorrected. ^{1}H and ^{13}C NMR spectra were determined at 270 and 67.8 MHz, respectively. Mass spectra and high-resolution mass spectra (HRMS) were determined on JEOL D-300 or JEOL DX-300. Specific rotations were measured on a JASCO DIP-360 digital polarimeter. CD spectra were taken on a JASCO 720W polarimeter. Analytical thin-layer chromatographies (TLC) were performed on precoated Kieselgel 60 F_{254}. Nonflash chromatography separations were performed on Kieselgel 60 (70−230 mesh) and flash chromatography on Kieselgel 60 (230−400 mesh). All solvents were purified and dried prior to use. All reactions sensitive to moisture or air were performed under Ar. All extracted solutions were dried over anhydrous Na_2SO_4 prior to evaporation.

Scheme 10[a]



[a] Reagents and conditions: (i) acetyl chloride, NaH, 18-crown-6, THF rt; (ii) CSA, MeOH−THF, rt; (iii) MnO_2, CH_2Cl_2, rt; (iv) propylmagnesium bromide THF, −10 °C; (v) *p*-TsOH, benzene, 50 °C; (vi) $NaBH_4$, MeOH, rt.

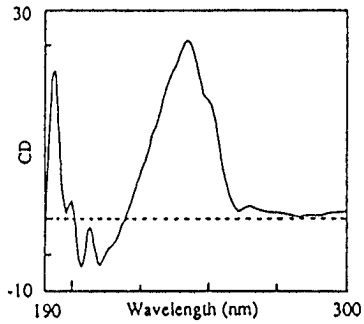


Figure 2. CD spectrum of *cis*-trikentrin B.

Synthesis of Menthyl Bicyclo[2.2.1]hepta-1,4-diene-1-carboxylate (15). A solution of **9** (436 mg, 1.09 mmol) in dry CH_2Cl_2 (10 mL) was treated with TFAA (0.31 mL) and 2,6-lutidine (0.258 mL, 2.19 mmol) under Ar. The reaction mixture was stirred at rt for 30 min. The resulting mixture was extracted with ether, and the combined organic layer was washed with 10% aqueous HCl solution, followed by saturated $NaHCO_3$ solution and then brine. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (10:1)] afforded **15** (416 mg, quantitative) as a colorless oil: HR FABMS calcd for $C_{23}H_{29}O_2NS$ 383.1919, found 383.1917; FABMS *m*/*z* (rel intensity) 384 (M + H$^+$, base), 383 (M$^+$, 47), 246 (73), 228 (58), 200 (34); IR ν_{max} ($CHCl_3$) cm^{-1} 1690; ^{1}H NMR ($CDCl_3$) δ 8.61 (1 H, ddd, J = 1.0, 4.9, 2.3 Hz), 7.67 (1 H, dt, J = 1.7, 7.6 Hz), 7.43 (1 H, ddd, J = 1.0, 7.6, 2.3 Hz), 7.23 (1 H, ddd, J = 1.0, 4.9, 7.4 Hz),

(19) Guida, W. C.; Mathre, D. J. *J. Org. Chem.* **1980**, *45*, 3172.

6.87 (1 H, dd, J = 3.0, 4.6 Hz), 6.74 (1 H, dd, J = 3.0, 4.6 Hz), 4.74 (1 H, dt, J = 4.3, 10.9 Hz), 4.02 (1 H, brs), 3.56 (1 H, brs), 2.22−0.76 (18 H, m); ^{13}C NMR ($CDCl_3$) δ 164.27, 156.46, 150.14, 143.08, 140.65, 137.56, 136.70, 126.96, 122.02, 74.24, 74.12, 69.89, 57.33, 51.37, 47.14, 41.33, 41.25, 34.34, 31.39, 26.44, 23.80, 21.99, 20.85, 20.74, 16.71; $[\alpha]^{28}_D$ −241.1 (*c* 0.53, $CHCl_3$).

Synthesis of Menthyl (1*S*)-2,2-Dimethoxybicyclo[2.2.1]-hept-4-ene-1-carboxylate (16). A solution of **15** (482 mg, 1.26 mmol) in dry methanol (26 mL) was treated with *p*-toluenesulfonic acid monohydrate (260 mg, 1.36 mmol) and trimethyl orthoformate (4.27 mL, 39.03 mmol). The reaction mixture was refluxed for 5 h. Then the solvent was removed in vacuo, and the resulting mixture was neutralized with saturated $NaHCO_3$ solution and extracted with ether. The combined organic layer was washed with brine, and the solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (10:1)] afforded **16** (268 mg, 63%) as a colorless oil: HR FABMS calcd for $C_{20}H_{32}O_4$ 336.2300, found 336.2301; FABMS m/z (rel intensity) 336 (M^+, 56), 305 (44), 270 (19), 181 (48), 167 (base); IR ν_{max} (neat) cm^{-1} 1735; ^{1}H NMR ($CDCl_3$) δ 6.60 (1 H, dd, J = 2.6, 5.6 Hz), 6.04 (1 H, dd, J = 3.0, 5.6 Hz), 4.65 (1 H, dt, J = 4.3, 10.9 Hz), 3.41 (1 H, s), 3.15 (1 H, s), 3.03 (1 H, d, J = 3.3 Hz), 2.98 (1 H, brs), 2.94 (1 H, brs), 2.00−0.75 (18 H, m); ^{13}C NMR ($CDCl_3$) δ 170.79, 139.02, 130.00, 113.11, 74.17, 54.86, 50.71, 50.32, 50.16, 47.27, 46.99, 44.05, 40.81, 34.38, 31.34, 26.31, 23.64, 22.03, 20.79, 16.56.

Synthesis of (1*R*)-2,2-Dimethoxybicyclo[2.2.1]hept-4-ene-1-ethanol (17). A solution of **16** (1.71 g, 5.08 mmol) in dry ether (20 mL) was treated with LAH (217 mg, 5.72 mmol) at 0 °C. The reaction mixture was warmed to rt and stirred for 30 min at rt. The resulting solution was quenched with saturated NH_4Cl solution and extracted with ether. The combined organic layer was washed with brine, and the solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (1:1)] afforded **17** (920 mg, 98%) as a colorless oil: HR FABMS calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1101; FABMS m/z (rel intensity) 184 (M^+, 18), 167 (base), 153 (74), 101 (63), 93 (33), 79 (22), 55 (13); IR ν_{max} (neat) cm^{-1} 3410; ^{1}H NMR ($CDCl_3$) δ 6.26 (1 H, dd, J = 3.0, 5.6 Hz), 6.08 (1 H, dd, J = 3.0, 5.6 Hz), 3.52 (1 H, ddd, J = 2.3, 5.9, 13.5 Hz), 3.34 (1 H, m), 3.30 (3 H, s), 3.22 (3 H, s), 2.93 (1H, brs), 2.72 (1 H, brs), 2.36 (2 H, m), 2.26 (1 H, dd, J = 4.0, 8.62 Hz), 1.75 (1 H, d, J = 9.2 Hz), 1.62 (1 H, dt, J = 2.0, 6.6 Hz); $[\alpha]^{25}_D$ −32.3 (*c* 1.0, $CHCl_3$).

Synthesis of (2*R*)-2-(Hydroxymethyl)norborn-4-en-1-one (18). A solution of **17** (6.35 g, 34.47 mmol) in THF (360 mL) was treated with 5% HCl solution (24 mL), and the reaction mixture was stirred at rt for 20 min. The solvent of the resulting mixture was removed in vacuo, and the residue was neutralized with $NaHCO_3$ powder. CH_2Cl_2 (100 mL) was added, the resulting solution was dried over anhydrous Na_2SO_4, and the solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (2:1)] afforded **18** (4.51 g, 95%) as a colorless oil: HR FABMS calcd for $C_8H_{11}O_2$ ($M + H^+$) 139.0759, found 139.0758; FABMS m/z (rel intensity) 139 ($M + H^+$, base), 138 (M^+, 9), 107 (10), 66 (28), 55 (5); IR ν_{max} (neat) cm^{-1} 3410, 1735; ^{1}H NMR ($CDCl_3$) δ 6.56 (1 H, dd, J = 2.6, 5.6 Hz), 6.08 (1 H, dd, J = 3.6, 4.6 Hz), 3.62 (1 H, dd, J = 10.9, 6.9 Hz), 3.49 (1 H, dd, J = 10.9, 6.9 Hz), 3.15 (1 H, t, J = 1.3 Hz), 3.11 (1 H, dd, J = 1.6, 3.3 Hz), 2.62(1H, brs), 2.39 (1 H, dt, J = 3.3, 7.1 Hz), 2.23 (1 H, d, J = 9.2 Hz), 2.00(1 H, d, J = 9.2 Hz); ^{13}C NMR ($CDCl_3$) δ 214.94, 140.80, 129.87, 64.86, 56.33, 50.09, 49.59, 41.94; $[\alpha]^{28}_D$ −720 (*c* 1.0, $CHCl_3$).

Synthesis of (2*R*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-norborn-4-en-1-one (8). A solution of **18** (4.51 g, 32.64 mmol) in dry CH_2Cl_2 (100 mL) was treated with *tert*-dimethylsilyl chloride (8.8 g, 58.4 mmol), imidazole (58.75 mmol), and a catalytic amount of DMAP. The reaction mixture was stirred at rt for 2 h. The resulting mixture was extracted with CH_2Cl_2, the combined organic layer was washed with brine, and the solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (1:1)] afforded **8** (7.28 g, 96%) as a colorless oil: HR FABMS calcd for $C_{14}H_{25}O_2Si$ ($M + H^+$) 253.1624, found 253.1616; FABMS m/z (rel intensity) 253 ($M + H^+$, base), 211 (37), 195 (93), 137 (50), 93 (34), 66 (11); ^{1}H NMR ($CDCl_3$) δ 6.53 (1 H, dd, J = 3.0, 5.6 Hz), 6.04 (1 H, dd, J = 3.0, 6.3 Hz), 3.86 (1 H, m), 3.21 (1 H, brs), 3.19−3.04 (2 H, m), 2.40−2.33 (1 H, m), 2.18 (1 H, brd, J = 9.2 Hz),1.91 (1 H, brd J = 9.2 Hz), 0.87 (9 H, s), 0.08(6 H, s); $[\alpha]^{25}_D$ −303 (*c* 0.53, $CHCl_3$).

Synthesis of (1*R*,2*S*)-Ethyl 2-[(*tert*-Butyldimethylsiloxy)methyl]-1-hydroxybicyclo[2.2.1]hept-4-ene-1-acetate (19). **8** (5 g, 19.81 mmol), zinc powder (17.5 g, 0.27 mol), and NH_4Cl powder (7.2 g, 0.13 mol) was mixed in a mortar and transferred to a steel dipper. Ethyl bromoacetate (12 mL, 0.05 mol) was added to the resulting mixture. After spontaneous exothermic reaction ceased, the resulting mixture was allowed to stand at rt for 2 h. The resulting hard cake was crushed, and saturated NH_4Cl solution was added and homogenized in a mortar. The resulting mixture was filtered off and washed with ethyl acetate. The mother liquor was extracted with ethyl acetate. The combined organic layer was washed with brine, and the solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (10:1)] afforded **19** (5.14 g, 85%) as a colorless oil: HR FABMS calcd for $C_{18}H_{33}O_4Si$ ($M + H^+$) 341.2148, found 341.2158; FABMS m/z (rel intensity) 341 ($M + H^+$, base), 323 (53), 283 (23), 257 (28), 217 (36), 73 (38); IR ν_{max} (neat) cm^{-1} 3520, 1740; ^{1}H NMR ($CDCl_3$) δ 6.29−6.26 (1 H, dd, J = 3.0, 5.3 Hz), 6.22−6.18 (1 H, dd, J = 3.0, 5.6 Hz), 4.22−4.15 (1 H, m), 3.59 (1 H, dd, J = 6.3, 10.2 Hz), 3.42 (1 H, dd, J = 7.9, 10.2 Hz), 3.35 (1 H, s), 2.95 (1 H, brs), 2.86 (1 H, brs),2.73 (2 H, q, J = 14.8 Hz), 2.06−2.00 (1 H, m), 1.56(1 H, s) 1.53 (1H, dd, J = 2.0, 9.2 Hz), 1.40 (H, d, J = 9.2 Hz), 1.29 (3 H, t, J = 7.3 Hz), 0.89 (9 H, s), 0.04 (6 H, d, J = 2.31 Hz); ^{13}C NMR ($CDCl_3$) δ 235.07, 172.34, 135.81, 134.97, 79.66, 63.77, 60.54, 52.84, 52.37, 47.20, 46.74, 45.20, 25.88, 18.15, 14.17.

Synthesis of (1*S*,4*R*)-Ethyl [3-[(*tert*-Butyldimethylsiloxy)methyl]bicyclo[2.2.1]hept-5-en-2-ylidene]-1-acetate (22). Thionyl chloride (7.5 mL, 102.82 mmol) was added dropwise to a solution of **19** (5 g, 14.68 mmol) in dry pyridine (300 mL) at 0 °C, and the reaction mixture was stirred at 0 °C for 15 min. The resulting mixture was neutralized with 10% sulfuric acid solution and extracted with ether. The combined organic layer was washed with saturated $NaHCO_3$ solution followed by brine. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (10:1)] afforded **22** (3.44 g, 73%) as a colorless oil: HR FABMS calcd for $C_{18}H_{31}O_3Si$ ($M + H^+$) 323.2042, found 323.2038; FABMS m/z (rel intensity) 323 ($M + H^+$, 54), 277 (58), 265 (base), 73 (51); IR ν_{max} (neat) cm^{-1} 1715. **22a**: ^{1}H NMR ($CDCl_3$) δ 6.33 (1 H, dd, J = 3.0, 5.6 Hz), 6.01 (1 H, dd, J = 3.0, 5.3 Hz), 5.85 (1 H, d, J = 2.0 Hz), 4.24 (1 H, dd, J = 4.6, 9.6 Hz), 4.14 (2 H, dd, J = 6.9, 14.2 Hz), 3.26 (2 H, dd, J = 1.7, 3.0 Hz), 3.20 (1 H, brs), 2.78 (1 H, t, J = 9.9 Hz), 1.74 (1 H, d, J = 8.6 Hz), 1.44 (1 H, d, J = 8.6 Hz), 1.26 (3 H, t, J = 7.1 Hz), 0.91 (9 H, s), 0.06 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 235.36, 166.45, 164.04, 137.98, 131.77, 112.38, 64.17, 59.74, 54.55, 49.80, 49.20, 44.16, 25.94, 18.22, 14.30. **22b**: ^{1}H NMR ($CDCl_3$) δ 6.19 (1 H, dd, J = 3.0, 5.6 Hz), 6.07−6.15 (1 H, m), 5.63 (1 H, d, J = 1.7 Hz), 4.52 (1 H, brs), 4.16 (2 H, q, J = 7.3 Hz), 3.56 (1 H, dd, J = 5.6, 9.9 Hz), 3.12 (2 H, t, J = 9.6 Hz), 3.06 (1 H, brs), 2.82−2.78 (1 H, m), 1.76 (1 H, brd, J = 8.9 Hz), 1.47 (1 H, brd, J = 8.9 Hz), 1.28 (3 H, t, J = 7.3 Hz), 0.91 (9 H, s), 0.05 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 235.08, 166.55, 165.47, 136.21, 133.29, 111.40, 66.86, 59.59, 49.80, 49.49, 48.99, 42.87, 42.41, 25.88, 18.25, 14.33, 14.20.

Synthesis of (1*S*,4*R*)-[3-[(*tert*-Butyldimethylsiloxy)-methyl]bicyclo[2.2.1]hept-5-en-2-ylidene]-1-ethanol (23). A solution of DIBALH (100 mL, 0.93 M in hexane solution) was added dropwise to a solution of **22** (10.96 g, 33.98 mmol) in dry ether (900 mL) at 0 °C under Ar. The reaction mixture was stirred at 0 °C for 2 h. The resulting mixture was quenched with 5% HCl and extracted with ether. The combined organic layer was washed with saturated $NaHCO_3$ solution, followed by brine. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (1:1)] afforded **23** (8.51 g, 89%) as a colorless

oil: HR FABMS calcd for $C_{20}H_{32}O_4$ 336.2300, found 336.2301; FABMS *m/z* (rel intensity) 253 ($M + H^+$, base), 211 (37), 195 (93), 137 (50), 93 (34), 66 (11); IR ν_{max} (neat) cm^{-1} 3325. **23a**: ^1H NMR ($CDCl_3$) δ 6.11 (2 H, brs), 5.63 (1 H, dt, J = 2.0, 6.9 Hz), 4.09 (2 H, d, J = 7.3 Hz), 3.56 (1 H, dd, J = 6.3, 10.0 Hz), 3.19 (1 H, dd, J = 8.6, 9.9 Hz),3.14 (1 H, brs), 3.05 (1 H, brs), 2.92−2.83 (1 H, m), 1.93 (1 H, brs), 1.62 (1 H, dt, J = 1.7, 8.3 Hz), 1.41 (1 H, dt, J = 1.7, 8.3 Hz), 0.91 (9 H, s), 0.06 (6 H, s). **23b**: ^1H NMR ($CDCl_3$) δ 6.13−6.01(1 H, m), 5.28 (1 H, t, J = 5.9 Hz), 4.33−4.11 (2 H, m), 3.65−3.54 (1 H, m), 3.48 (1 H, brd, J = 7.6 Hz), 3.06 (1 H, brt), 2.72 (1 H, brm), 1.68 (1 H, m), 1.43 (2 H, m), 0.91 (9 H, s), 0.04 (6 H, s).

Synthesis of (1*R*,4*S*)-3-[2-(Triphenylmethoxy)ethylidene]-3-[(*tert*-butyldimethylsiloxy)methyl]bicyclo[2.2.1]-hept-5-ene (21). A solution of **23** (3.8 g, 13.55 mmol) in dry CH_2Cl_2 (290 mL) was treated with TrCl (16 g, 57 mmol), triethylamine (19 mL, 260 mmol), and DMAP (870 mg, 7.12 mmol). The reaction mixture was stirred at rt for 10 h. The resulting mixture was poured into ice−water and extracted with CH_2Cl_2. The combined organic layer was washed with NH_4Cl solution, followed by water and then brine. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (20:1)] afforded **21** (6.46 g, 91%) as a colorless oil: HR FABMS calcd for $C_{35}H_{43}O_2Si$ ($M + H^+$) 523.3032, found 523.3028; FABMS *m/z* (rel intensity) 523 ($M + H^+$, 1), 243 (base); IR ν_{max} (neat) cm^{-1} no characteristic peak; ^1H NMR ($CDCl_3$) δ 7.46−7.42 (6 H, m), 7.32−7.19 (9 H, m), 6.10 (2 H, t, J = 1.7 Hz), 5.63 (1 H, t, J = 5.3 Hz), 3.19 (1 H, dd, J = 8.6, 9.9 Hz),3.14 (1 H, brs), 3.05 (1 H, brs), 2.92−2.83 (1 H, m), 3.62−3.44 (2 H, m), 3.37 (1 H, dd, J = 5.0, 10.2 Hz), 3.14−3.13 (1 H, m), 3.05 (1 H, brs), 2.78 (1 H, dd, J = 9.9, 10.9 Hz), 2.66−2.55 (1 H, m), 1.60 (1 H, brd, J = 8.2 Hz), 1.37 (1 H, brd, J = 8.2 Hz), 0.83 (9 H, s), −0.11 (6 H, d, J = 5.3 Hz).

Synthesis of (1*R*,4*S*)-3-[2-(Triphenylmethoxy)ethylidene]bicyclo[2.2.1]hept-5-en]-1-ethanol (24). 21 (6.46 g, 12.36 mmol) was treated with a solution of tetrabutylammonium fluoride (28 mL, 1.1 M solution in THF). The reaction mixture was stirred at rt for 5 h. Brine was added, and the resulting mixture was extracted with ethyl acetate. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (5:1)] afforded **24** (4.85 g, 96%) as a colorless oil: HR FABMS calcd for $C_{29}H_{28}O_2Na$ ($M + Na^+$) 431.1897, found 431.1986; FABMS *m/z* (rel intensity) 431 ($M + Na^+$, 4), 243 (base), 165 (59), 154 (26); IR ν_{max} (neat) cm^{-1} 3400. **21a**: ^1H NMR ($CDCl_3$) δ 7.47−7.42 (6 H, m), 7.32−7.19 (9 H, m), 6.14 (2 H, t, J = 1.7 Hz), 5.67 (1 H, dt, J = 2.0, 6.9 Hz), 3.63 (1 H, dd, J = 7.3, 10.9 Hz), 3.49 (1 H, dd, J = 6.6, 10.9 Hz), 3.36−3.30 (1 H, m), 3.19−3.17 (1 H, m), 3.10−3.00 (3 H, m), 2.70−2.58 (1 H, m), 1.62 (1 H, brd, J = 8.3 Hz), 1.38 (1 H, brd, J = 8.3 Hz). **21b**: ^1H NMR ($CDCl_3$) δ 7.48−7.43 (6 H, m), 7.33−7.19 (9 H, m), 6.08 (1 H, dd, J = 3.0, 5.6 Hz), 5.95 (1 H, dd, J = 3.0, 5.6 Hz), 5.88 (0.5 H, dd, J = 3.0, 5.6 Hz), 5.78 (0.5 H, dd, J = 3.0, 5.6 Hz), 3.68−3.60 (2 H, m), 3.21−3.13 (2 H, m),3.04 (1 H, brs), 2.76−2.72 (1 H, m), 1.60 (1 H, brd, J = 8.2 Hz), 1.40 (1 H, brd, J = 8.3 Hz).

Synthesis of (1*R*,4*S*)-3-[2-(Triphenylmethoxy)ethylidene]-3-[(*tert*-butyldimethylsiloxy)methyl]bicyclo[2.2.1]-hept-5-ene]-1-carbaldehyde (7). A solution of **23** (4.85 g, 11.87 mmol) in CH_2Cl_2 (75 mL) was treated with PCC (3.5 g, 160 mmol) and celite (1.87 g). The reaction mixture was stirred at rt for 3 h. The resulting solution was diluted with ether, passed through a Florisil column, and washed with ether. The eluent was collected, and the solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (5:1)] afforded **7** (3.3 g, 68%) as a colorless oil: HR FABMS calcd for $C_{20}H_{32}O_4$ 336.2300, found 336.2301; FABMS *m/z* (rel intensity); IR ν_{max} (neat) cm^{-1} 1710. **7a**: ^1H NMR ($CDCl_3$) δ 9.01 (1 H, d, J = 4.3 Hz), 7.48−7.43 (6 H, m), 7.33−7.23 (9 H, m), 6.22 (1 H, dd, J = 3.0, 5.6 Hz), 6.02 (1 H, dd, J = 3.3, 5.3 Hz), 5.42 (1 H, t, J = 5.9 Hz), 3.72−3.67(2 H, m), 3.38 (1 H, brs), 3.23 (1 H, brs), 1.65 (1 H, t, J = 1.7 Hz), 1.62 (1 H, t, J = 1.7 Hz), 1.44 (1 H, brd, J = 8.6 Hz). **7b**: ^1H NMR ($CDCl_3$) δ 9.82 (1 H, d, J = 8.2 Hz), 7.45−7.41 (6 H, m), 7.33−7.22 (9 H, m), 5.96 (1 H, dd, J = 2.6, 5.6 Hz), 5.90−5.87 (1 H, m), 5.72 (1 H, brd, J = 7.6 Hz), 4.12 (1 H, brs, J = 3.0, 5.6 Hz), 3.29 (1 H, brs), 3.20 (1 H, dd, J = 5.0, 9.2 Hz), 3.00−2.96 (1 H, m), 2.58 (1 H, t, J = 9.2 Hz), 1.87 (1 H, brd, J = 8.9 Hz), 1.56 (1 H, brd, J = 8.9 Hz), 1.26 (1 H, d, J = 3.0 Hz), 0.88 (1 H, t, J = 6.9 Hz).

Methyl (1*S*,4*R*)-3-(Hydroxymethyl)bicyclo[2.2.1]hept-5-ene-2-ylideneacetate (27). A solution of **26**[11] (110 mg, 0.68 mmol) in dry benzene (100 mL) was treated with Fetizon reagent (4.15 g, *ca.* 4.15 mmol), and the resulting mixture was refluxed under Ar for 1 h. After being cooled to rt, the reaction mixture was filtered, the solvent was removed in vacuo, and the resulting residue was used for the subsequent reaction without further purification. A suspension of the crude lactone and $LiOH·H_2O$ (60 mg, 1.4 mmol) in THF and water (2:1, 15 mL) was stirred at rt for 90 min. Water was added, and the aqueous layer was washed with hexane. The resulting water layer was acidified to pH 5 with 10% HCl and extracted with ether. The solvent was removed in vacuo. The thus obtained residue was used in the subsequent reaction without further purification. (Trimethylsilyl)diazomethane in ether was added to a stirred solution of the residue in methanol (2 mL) and benzene (7 mL). The reaction mixture was stirred at rt until the starting material disappeared on TLC, and the solvent of the resulting mixture was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (1:1)] afforded **27** (72.5 mg, 54% from **26**) as a yellow oil: HR FABMS calcd for $C_{11}H_{15}O_3$ ($M + H^+$) 195.1022, found 195.1016; EIMS *m/z* (rel intensity) 194 (M^+, 38), 117 (base); IR ν_{max} ($CHCl_3$) cm^{-1} 3450, 1700; ^1H NMR ($CDCl_3$) δ 6.37 (1H, dd, J = 5.5, 2.3 Hz), 6.06 (1H, dd, J = 5.5, 3.1 Hz), 5.94 (1H, s), 3.83−3.74 (1H, m), 3.70 (3H, s), 3.39 (1H, brs), 3.33 (1H, d, J = 1.7 Hz), 3.19 (3H, brs), 1.73 (1H, brd, J = 8.9 Hz), 1.47 (1H, brd, J = 8.9 Hz); $[\alpha]^{24}_D$ −306.2 (*c* 1.2, $CHCl_3$).

Methyl (1*S*,4*R*)-3-[(*tert*-Butyldimethylsiloxy)methyl]-bicyclo[2.2.1]heptene-2-ylideneacetate (28). In a manner similar to the synthesis of **8**, **28** (2.34 g, 94%) was obtained as a colorless oil from the alcohol **27** (1.55 g, 8.04 mmol): HR FABMS calcd for $C_{17}H_{29}O_3Si$ ($M + H^+$) 309.1887, found 309.1886; EIMS *m/z* (rel intensity) 308 (M^+, 3.8); IR ν_{max} ($CHCl_3$) cm^{-1} 1710; ^1H NMR ($CDCl_3$) δ 6.33 (1H, dd, J = 5.6, 3.0 Hz), 6.01 (1H, dd, J = 5.6, 3.3 Hz), 5.86 (1H, d, J = 2.3 Hz), 4.25 (1H, dd, J = 9.4, 5.0 Hz), 3.69 (3H, s), 3.29−3.20 (3H, m), 2.78 (1H, t, J = 10.2 Hz), 1.73 (1H, brd, J = 8.6 Hz), 1.44 (1H, brd, J = 8.6 Hz), 0.91 (9H, s), 0.06 (6H, d, J = 7.9 Hz); $[\alpha]^{25}_D$ −161.9 (*c* 1.4, $CHCl_3$).

(1*S*,4*R*)-3-[(*tert*-Butyldimethylsiloxy)methyl]bicyclo-[2.2.1]hept-5-ene-2-ylideneethanol (23a). A solution of **28** (114 mg, 0.683 mmol) in dry CH_2Cl_2 (10 mL) was cooled to −78 °C, and a 0.93 M solution of DIBALH in hexane (1.5 mL, 1.4 mmol) was added dropwise. The mixture was stirred at −78 °C for 2.5 h, warmed to 0 °C, and quenched with saturated aqueous NH_4Cl solution. The resulting slurry was acidified to pH 5 with 10% HCl and extracted with CH_2Cl_2. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (4:1)] afforded **23a** (164 mg, quantitative) as a pale yellow oil: $[\alpha]^{24}_D$ −178.6 (*c* 1.4, $CHCl_3$).

(1*R*,4*S*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-3-[2-(triphenylmethoxy]ethylidene]bicyclo[2.2.1]hept-5-ene (21a). In a manner similar to the synthesis of **21**, **21a** (2.40 g, 87%) was obtained as a colorless oil from **23a** (1.46 g, 5.24 mmol).

(1*R*,4*S*)-3-[2-(Triphenylmethoxy)ethylidene]bicyclo-[2.2.1]hept-5-ene-2-methanol (24a). In a manner similar to the synthesis of **24**, **24a** (0.193 g, 97%) was obtained as a colorless oil from **21a** (0.256 g, 0.49 mmol): $[\alpha]^{24}_D$ −137.8 (*c* 1.2, $CHCl_3$).

(1*R*,4*S*)-3-[2-(Triphenylmethoxy)ethylidene]bicyclo-[2.2.1]hept-5-ene-2-carboxaldehyde (7a). In a manner similar to the synthesis of **7**, **7a** (1.16 g, 77%) was obtained as a colorless oil from **24a** (1.93 g, 3.66 mmol): $[\alpha]^{25}_D$ −86.9 (*c* 1.0, $CHCl_3$).

Synthesis of 2,2-Dimethyl-*N*-propynyl-*N*-[(1*R*,8*S*)-[3-[(2-triphenylmethoxy)ethylidene]bicyclo[2.2.1]hept-5-en-2-ylidene]methyl]propionamide (6). Propargylamine (0.9 mL, 13.12 mmol) was added dropwise to a solution of **7** (3.04 g, 7.48 mmol) and molecular sieves 4A (12.2 g) in dry ether (45 mL) at 0 °C. The reaction mixture was warmed to

rt and stirred at rt for 5 h. The resulting solution was filtered, and the solvent was removed in vacuo. The residue was dissolved in dry CH_2Cl_2 (60 mL) and cooled to 0 °C. 2,4,6-Collidine (4.1 mL, 31.03 mmol) and then trimethylacetyl chloride (1.9 mL, 15.43 mmol) were added dropwise to the resulting solution. The reaction mixture was warmed to rt and stirred at rt for 10 h. The resulting solution was extracted with CH_2Cl_2, and the combined organic layer was washed with 10% aqueous HCl solution, followed by saturated $NaHCO_3$ solution and then brine. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (10:1)] afforded **6** (2.20 g, 56%) as a colorless oil: HR FABMS calcd for $C_{37}H_{38}O_2N$ ($M + H^+$) 528.2902, found 528.2897; FABMS *m/z* (rel intensity) 528 ($M + H^+$, 58), 284 (69), 243 (base), 165 (45); IR ν_{max} (neat) cm^{-1} 2250, 1630. **6a:** ^1H NMR ($CDCl_3$) δ 7.54−7.42 (6 H, m), 7.35−7.19 (9 H, m), 6.38 (1 H, dd, $J = 3.0, 5.1$ Hz), 6.22−6.18 (1 H, m), 5.99 (1 H, t, $J = 5.3$ Hz), 4.12 (1 H, dd, $J = 2.3, 16.7$ Hz), 4.00 (1 H, dd, $J = 2.3, 16.7$ Hz), 3.80 (2 H, d, $J = 5.3$ Hz), 3.60(1 H, brs), 2.07 (1 H, t, $J = 2.3$ Hz), 1.79−1.75(1 H, m), 1.02 (9 H, s). **6b:** ^1H NMR ($CDCl_3$) δ 7.54−7.42 (6 H, m), 7.35−7.19 (9 H, m), 6.61 (1 H, s), 6.22−6.18 (1 H, m), 5.85 (1 H, t, $J = 6.6$ Hz), 4.20 (1 H, d, $J = 2.6$ Hz), 4.17 (1 H, d, $J = 2.6$ Hz), 3.83−3.78 (2 H, m), 3.66 (1 H, brs), 3.40 (1 H, brs), 2.23 (1 H, t, $J = 2.6$ Hz), 1.62−1.58(1 H, m), 1.49−1.46(1 H, m), 1.23 (9 H, s).

Synthesis of Allenic Dienamide 25. A solution of **6** (2.20 g, 4.17 mmol) in 1,4-dioxane (100 mL) was treated with formalin (34% solution, 1.63 mL, 19 mmol), diisopropylamine (2 mL, 14.27 mmol), and CuBr (533 mg, 3.72 mmol). The reaction mixture was refluxed for 5 h. The resulting mixture was cooled to rt, diluted with ethyl acetate, and filtered. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (10:1)] afforded **25** (1.25 g, 56%) as a colorless oil: HR FABMS calcd for $C_{38}H_{40}O_2N$ ($M + H^+$) 542.3059, found 542.3067; FABMS *m/z* (rel intensity); IR ν_{max} (neat) cm^{-1} 1950, 1600; ^1H NMR ($CDCl_3$) δ 7.46−7.41 (6 H, m), 7.32−7.22 (9 H, m), 6.37 (1 H, dd, $J = 3.0, 5.3$ Hz), 6.17 (1 H, dd, $J = 3.0, 5.3$ Hz), 5.99 (1 H, s), 5.95 (1 H, d, $J = 5.3$ Hz), 5.07 (1 H, t, $J = 6.6$ Hz), 4.55 (1 H, t, $J = 3.0$ Hz), 4.52 (1 H, t, $J = 3.0$ Hz), 4.18 (0.5 H, t, $J = 3.0$ Hz), 4.12 (0.5 H, t, $J = 3.0$ Hz), 3.79 (1 H, dd, $J = 4.3, 5.6$ Hz), 3.51 (1 H, brs), 3.31 (1 H, brs), 1.77 (0.5 H, brs), 1.74 (0.5 H, brs), 1.62 (1 H, brs), 1.58 (1 H, d, $J = 8.6$ Hz), 1.01 (9 H, s).

Synthesis of (6*S*,9*R*)-1-(2,2-Dimethyl-1-oxopropyl)-2,4,5,6,9,9b-hexahydro-5-[(triphenylmethoxy)methyl]-6,9-methano-1*H*-benz[*g*]indole (29). A solution of **25** (1.24 g, 2.29 mmol) in toluene (30 mL) was heated at 160 °C in a sealed tube for 7 h. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (4:1)] afforded **33** (1.1 g, 88%) as a colorless oil: HR FABMS calcd for $C_{38}H_{40}O_2N$ ($M + H^+$) 542.3059, found 542.3060; FABMS *m/z* (rel intensity) 542 ($M + H^+$, 14), 541 (M^+, 11), 299 (23), 298 (72), 243 (base), 241 (9), 165 (38); IR ν_{max} (neat) cm^{-1} 1620. **29a:** ^1H NMR ($CDCl_3$) δ 7.48−7.42 (6 H, m), 7.36−7.20 (9 H, m), 6.61−6.57 (2 H, m), 5.56 (1 H, brs), 5.15 (1 H, brs), 4.45 (1 H, dd, $J = 1.7, 13.5$ Hz), 4.18 (1 H, dd, $J = 4.0, 13.5$ Hz), 3.74 (1 H, brs), 3.33 (1 H, dd, $J = 4.0, 8.9$ Hz), 3.18 (1 H, dd, $J = 4.0, 8.9$ Hz), 3.01 (1 H, brs), 2.28−2.23 (1 H, m), 1.30 (9 H, s). **29b**: ^1H NMR ($CDCl_3$) δ 7.46−7.42 (6 H, m), 7.34−7.24 (9 H, m), 6.45 (1 H, dd, $J = 3.0, 5.0$ Hz), 6.25 (1 H, dd, $J = 3.0, 5.0$ Hz), 5.46 (1 H, brs), 4.88 (1 H, brs), 4.36 (1 H, dd, $J = 3.0, 13.5$ Hz), 4.02 (1 H, dd, $J = 4.6, 13.2$ Hz), 3.68 (1 H, brs), 3.00 (1 H, brs), 2.91 (1 H, dd, $J = 3.0, 8.6$ Hz), 2.89−2.79 (1 H, m), 2.70−2.58 (1 H, m), 2.50−2.40 (1 H, m), 1.79 (2 H, brd, $J = 5.9$ Hz), 1.62 (2 H, brs), 1.25 (9 H, s).

Synthesis of (6*S*,9*R*)-1-(2,2-Dimethyl-1-oxopropyl)-,6,9-dihydro-5-[(triphenylmethoxy)methyl]-6,9-methano-1*H*-benz[*g*]indole (5). A solution of **29** (1.05 g, 1.94 mmol) in dry CH_2Cl_2 (35 mL) was treated with active MnO_2 (5.3 g, 61 mmol). The reaction mixture was stirred at rt for 10 h. The resulting mixture was filtered, and the solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (10:1)] afforded **5** (877 mg, 85%) as a colorless oil: HR FABMS calcd for $C_{38}H_{35}O_2N$ 537.2668, found 537.2677; FABMS *m/z* (rel intensity) 537 (M^+, base), 278 (39), 243 (98); IR ν_{max} (neat) cm^{-1} 1400; ^1H NMR ($CDCl_3$) δ 7.61−7.44 (8 H, m), 7.35−7.21 (9 H, m), 7.03 (1 H, dd, $J = 3.0, 5.3$ Hz), 6.81 (1 H, dd, $J = 3.0, 5.3$ Hz), 6.57 (1 H, d, $J = 4.0$ Hz), 4.59 (1 H, brs), 4.21 (2 H, s), 3.84 (1 H, brs), 2.18 (1 H, dt, $J = 1.7, 7.0$ Hz), 2.12 (2 H, brd, $J = 7.0$ Hz), 1.53 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 176.84, 150.04, 144.37, 143.80, 138.97, 131.58, 128.84, 127.80, 126.96, 128.25, 125.62, 116.12, 108.52, 87.01, 68.35, 64.26, 51.79, 48.59, 41.19, 31.58, 29.14, 22.64, 14.08; $[\alpha]^{28}_D$ +45 (*c* 1.0, $CHCl_3$).

Synthesis of (6*S*,9*R*)-1-(2,2-Dimethyl-1-oxopropyl)-6,7,8,9-tetrahydro-5-[(triphenylmethoxy)methyl]-7,8-dihydroxy-6,9-methano-1*H*-benz[*g*]indole (30). A solution of **5** (273 mg, 0.51 mmol) in 1,4-dioxane, water, and ether (5:1:1, 22 mL) was treated with osmium tetraoxide (2 g/L, 5 mL), pyridine (0.25 mL), NMO (250 mg, 2.13 mmol), and methanesulfonamide (105 mg, 1.10 mmol). The reaction mixture was stirred at rt for 5 h. A solution of saturated sodium bisulfite was added to the reaction mixture, and the resulting solution was stirred at rt for 30 min. The resulting solution was extracted with ethyl acetate, and the combined organic layer was washed with 2 N aqueous KOH solution and then brine. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (2:1)] afforded **30** (260 mg, 90%) as a colorless oil: HR FABMS calcd for $C_{38}H_{37}O_4N$ 571.2722, found 571.2726; FABMS *m/z* (rel intensity) 571 (M^+, 11), 554 (13), 511 (22), 328 (4), 243 (base); IR ν_{max} (neat) cm^{-1} 3475, 1690; ^1H NMR ($CDCl_3$) δ 7.59 (1 H, d, $J = 3.6$ Hz), 7.55−7.60 (6 H, m), 7.47 (1 H, s), 7.39−7.21 (9 H, m), 6.61 (1 H, d, $J = 4.0$ Hz), 4.24 (2 H, brs), 4.24−4.18 (1 H, m), 3.82−3.72 (1 H, m), 3.32 (1 H, brs), 3.21 (1 H, m), 3.12 (1 H, d, $J = 1.1$ Hz), 2.14 (1 H, d, $J = 9.9$ Hz), 1.88 (1 H, brs), 1.74 (1H, d, $J = 9.9$ Hz), 1.52 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 177.17, 144.19, 142.30, 131.38, 131.17, 129.37, 128.75, 128.84, 127.02, 125.59, 117.93, 108.45, 87.20, 71.13, 71.03, 67.08, 64.01, 60.35, 51.34, 48.55, 41.52, 41.25, 28.94, 14.17; $[\alpha]^{28}_D$ +1.8 (*c* 0.6, $CHCl_3$).

Synthesis of (6*R*,8*S*)-1-(2,2-Dimethyl-1-oxopropyl)-5-[(triphenylmethoxy)methyl]-6,8-diformyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (4). A solution of **30** (210 mg, 0.37 mmol) in THF and water (24:7, 31 mL) was treated with sodium periodate (1.3 g/L,6.08 mmol). The reaction mixture was stirred at rt for 1 h. Brine was added, and the resulting solution was extracted with ethyl acetate. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (3:1)] afforded **4** (200 mg, 96%) as a colorless oil: HR FABMS calcd for $C_{38}H_{35}O_4N$ 569.2566, found 569.2574; FABMS *m/z* (rel intensity) 569 (M^+, 1), 556 (4), 540 (8), 243 (base); IR ν_{max} (neat) cm^{-1} 1730; ^1H NMR ($CDCl_3$) δ 9.68 (1H, d, $J = 0.7$ Hz), 9.38 (1H, d, $J = 2.0$ Hz), 7.73 (1H, s), 7.68 (1H, d, $J = 4.0$ Hz), 7.53−7.48 (6 H, m), 7.35−7.22 (9 H, m), 6.71 (1 H, d, $J = 4.0$ Hz), 4.81 (1 H, dd, $J = 2.0, 10.2$ Hz), 4.21 (2 H, dd, $J = 5.3, 11.2$ Hz), 3.91 (1 H, dt, $J = 1.7, 9.2$ Hz), 2.74 (1 H, dt, $J = 2.0, 13.5$ Hz), 2.61−2.49 (1 H, m), 1.49 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 200.54, 199.54, 177.81, 143.86, 136.08, 133.51, 131.26, 131.07, 128.79, 128.69, 127.94, 127.16, 126.67, 126.18, 121.07, 107.83, 87.53, 64.32, 57.68, 55.60, 41.52, 31.58, 28.82, 27.32, 22.64, 14.08.

Synthesis of (6*R*,8*S*)-5-[(Triphenylmethoxy)methyl]-6,8-bis(hydroxymethyl)-1,6,7,8-tetrahydrocyclopent[*g*]-indole (34). A solution of **4** (200 mg, 0.35 mmol) in methanol (12 mL) was treated with sodium borohydride (100 mg, 2.64 mmol). The reaction mixture was stirred at rt for 2 h. The solvent was removed in vacuo. Water was added to the residue and extracted with ether. The combined organic layer was washed with brine; and the solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (1:2)] afforded **34** (152 mg, 88%) as a colorless oil: HR FABMS calcd for $C_{33}H_{31}O_3N$ 489.2304, found 489.2299; FABMS *m/z* (rel intensity) 489 (M^+, 26), 307 (22), 289 (11), 243 (base), 230 (16); IR ν_{max} (neat) cm^{-1} 3350; ^1H NMR ($CDCl_3$) δ 9.54 (1H, brs), 7.62 (1H, s), 7.57−7.52 (6 H, m), 7.49−7.21 (9 H, m), 7.15−7.13 (1 H, m), 6.56 (1 H, dd, $J = 2.0, 3.3$ Hz), 4.30 (1 H, d, $J = 10.2$ Hz), 4.14 (1 H, d, $J = 3.6$ Hz), 4.10 (1 H, t, $J = 7.3$ Hz), 3.96−3.92 (1 H, m), 3.77 (1 H, t, $J = 9.9$ Hz), 3.49−3.51 (1 H, m), 3.43 (2 H, d, $J = 4.3$ Hz), 3.31−3.23 (1 H, dt, $J = 4.6, 13.2$ Hz), 2.45−2.33 (1 H, m), 2.03 (2 H, s), 1.66 (1 H, dt, $J = 5.6, 13.2$ Hz), 1.25 (2 H, t, $J = 7.3$

Hz); ^{13}C NMR ($CDCl_3$) δ 143.99, 143.66, 135.80, 135.63, 133.57, 129.31, 129.25, 129.20, 128.80, 127.24, 127.05, 128.68, 128.08, 127.91, 127.67, 127.61, 127.53, 127.32, 127.25, 127.14, 126.08, 124.48, 124.25, 123.87, 121.22, 121.04, 102.50, 102.25, 87.49, 87.45, 69.45, 68.19, 68.14, 67.14, 65.90, 65.43, 65.30, 65.16, 64.71, 60.38, 46.60, 45.42, 43.42, 32.53, 32.48, 21.00, 14.19, 11.00.

Synthesis of (6*R*,8*S*)-5-[(Triphenylmethoxy)methyl]-6,8-bis[(mesyloxy)methyl]-1,6,7,8-tetrahydrocyclopent-[*g*]indole (35). Methanesulfonyl chloride (0.15 mL, 1.94 mmol) was added dropwise to a solution of **34** (142 mg, 0.29 mmol) in dry ether (50 mL) and triethylamine (3 mL, 21.52 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 4 h. Water was added and extracted with CH_2Cl_2. The solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (1:1)] afforded **35** (155 mg, 83%) as a colorless oil: HR FABMS calcd for $C_{35}H_{35}O_7NS_2$ 645.1855, found 645.1845; FABMS *m*/*z* (rel intensity) 645 (M^+, 19), 386 (11), 243 (base), 154 (85), 136 (66); IR ν_{max} (neat) cm^{-1} 3475; ^{1}H NMR ($CDCl_3$) δ 8.83 (1H, brs), 7.64 (1H, s), 7.56−7.51 (6 H, m), 7.37−7.21 (10 H, m), 6.61 (1 H, dd, J = 2.0, 3.0 Hz), 4.60 (1 H, dd, J = 6.0, 9.9 Hz), 4.46 (1 H, t, J = 9.6 Hz), 4.37 (1 H, dd, J = 3.3, 9.9 Hz), 4.27 (1 H, d, J = 10.6 Hz), 4.09 (1 H, d, J = 10.6 Hz), 3.97 (1 H, dd, J = 7.0, 9.7 Hz), 3.92−3.82 (1 H, m), 3.62−3.52 (1 H, m), 2.98 (3 H, s), 2.70−2.55 (1 H, m), 2.56 (3 H, s), 1.98 (1 H, dm, J = 14.5 Hz); ^{13}C NMR ($CDCl_3$) δ 143.90, 134.67, 132.90, 128.80, 128.73, 128.54, 127.17, 127.99, 126.21, 126.97, 125.18, 122.13, 102.96, 87.46, 74.94, 73.30, 65.00, 45.16, 43.12, 37.38, 36.77, 31.51, 31.12; $[\alpha]^{24}_D$ +2.1 (*c* 0.4, $CHCl_3$).

Synthesis of (6*R*,8*S*)-5-[(Triphenylmethoxy)methyl]-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (36). A solution of **35** (145 mg, 0.22 mmol) in dry DME (16 mL) was treated with NaI (903 mg, 6.02 mmol) and zinc (4 g, 61.2 mmol). The reaction mixture was refluxed for 5 h under Ar. The resulting mixture was filtered and extracted with CH_2Cl_2. The combined organic layer was washed with brine, and the solvent was removed in vacuo. Purification of the residue by column chromatography [hexane−ethyl acetate (8:1)] afforded **36** (71.2 mg, 69%) as a white powder: 155 °C dec; HR FABMS calcd for $C_{33}H_{31}ON$ 457.2405, found 457.2410; FABMS *m*/*z* (rel intensity) 457 (M^+, 27), 243 (base), 214 (16); IR ν_{max} (neat) cm^{-1} 3500; ^{1}H NMR ($CDCl_3$) δ 8.00 (1H, brs), 7.73 (1H, s), 7.58−7.49 (6 H, m), 7.36−7.16 (10 H, m), 6.62 (1 H, dd, J = 2.0, 3.3 Hz), 4.23 (2 H, s), 3.48−3.38 (1 H, m), 3.29−3.17 (1 H, m), 2.62 (1 H, dt, J = 8.9, 12.9 Hz), 1.44 (3 H, d, J = 6.9 Hz), 1.45−1.35 (1 H, m), 1.03 (3 H, d, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 144.45, 140.90, 132.12, 129.56, 128.88, 127.73, 127.33, 127.18, 126.87, 123.55, 118.96, 103.23, 86.94, 64.37, 60.36, 42.62, 38.82, 36.93, 23.38, 22.23; $[\alpha]^{27}_D$ +6.2 (*c* 0.4, $CHCl_3$).

Synthesis of (6*R*,8*S*)-1-(Phenylsulfonyl)-5-[(triphenylmethoxy)methyl]-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (38). A solution of **36** (10 mg, 0.02 mmol) in dry THF was treated with NaH (60%, 5 mg, 0.125 mmol) and 18-crown-6 (9.3 mg, 0.035 mmol). The resulting mixture was cooled to 0 °C, benzenesulfonyl chloride (0.004 mL, 0.03 mmol) was added dropwise, and the reaction mixture was stirred overnight at rt. Saturated $NaHCO_3$ solution was added, and the resulting solution was extracted with CH_2Cl_2. The combined organic layer was washed with brine, and the solvent was removed in vacuo. Purification of the residue by flash column chromatography [hexane−ethyl acetate (8:1)] afforded **38** (8.8 mg, 68%) as a colorless oil: HR FABMS calcd for $C_{39}H_{35}O_3NS$ 597.2337, found 597.2344; FABMS *m*/*z* (rel intensity) 597 (M^+, 3), 457 (11), 243 (base); IR ν_{max} ($CHCl_3$) cm^{-1} 3620; ^{1}H NMR ($CDCl_3$) δ 7.73 (1H, d, J = 4.6 Hz), 7.66−7.44 (8 H, m), 7.40−7.13 (14 H, m), 6.76 (1 H, d, J = 3.6 Hz), 4.16−4.03 (2 H, m), 3.01−2.95 (1 H, m), 2.45−2.34 (1 H, m), 1.50−1.35 (1 H, m), 1.31 (3 H, d, J = 6.9 Hz), 1.00 (3 H, d, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$) δ 144.09, 134.81, 133.29, 131.73, 129.55, 129.33, 129.04, 128.70, 127.81, 127.17, 127.02, 126.42, 123.52, 118.95, 111.14, 103.21, 86.88, 63.27, 41.24, 38.61, 37.38, 23.51, 23.35; $[\alpha]^{24}_D$ +98.8 (*c* 1.4, $CHCl_3$).

Synthesis of (6*R*,8*S*)-1-(Phenylsulfonyl)-5-(hydroxymethyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (39) (Method 1). A solution of **38** (8.8 mg, 0.015 mmol) in methanol and THF (1:1, 1 mL) was treated with 10-camphorsulfonic acid (5 mg, 0.01 mmol). The reaction mixture was stirred for 5 h at rt. Saturated $NaHCO_3$ solution was added, and the resulting solution was extracted with CH_2Cl_2. The combined organic layer was washed with brine, and the solvent was removed in vacuo. Purification of the residue by flash column chromatography [hexane−ethyl acetate (2:1)] afforded **39** (4 mg, 77%) as a colorless oil: HR FABMS calcd for $C_{20}H_{21}O_3NS$ 355.1242, found 355.1240; FABMS *m*/*z* (rel intensity) 356 (M + H^+, base), 281 (M^+, 32); IR ν_{max} ($CHCl_3$) cm^{-1} 3620; ^{1}H NMR ($CDCl_3$) δ 7.61 (1 H, d, J = 4.0 Hz), 7.57−7.65 (2 H, m), 7.31−7.50 (4 H, m), 6.68 (1 H, d, J = 3.6 Hz), 4.83 (1 H, d, J = 12.5 Hz), 4.72 (1 H, d, J = 12.5 Hz), 4.12 (1 H, dq, J = 7.0, 8.6 Hz), 3.38 (1 H, dd, J = 7.3, 8.6 Hz), 2.51 (1 H, ddd, J = 8.9, 8.9, 12.5 Hz), 1.61 (1 H, s), 1.56 (1 H, d, J = 12.5 Hz), 1.36 (3 H, d, J = 6.9 Hz), 1.34 (3 H, d, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 135.33, 133.48, 133.36, 132.51, 129.66, 129.08, 126.40, 119.25, 110.95, 77.22, 76.80, 62.77, 41.22, 38.74, 37.50, 23.62, 23.56; $[\alpha]^{28}_D$ +616.3 (*c* 0.3, $CHCl_3$).
Method 2. A solution of **36** (10 mg, 0.02 mmol) in dry DME (0.4 mL) was treated with NaH (60%, 5 mg, 0.125 mmol). The reaction mixture was stirred at rt for 30 min under Ar. Benzenesulfonyl chloride (0.004 mL, 0.03 mmol) was added dropwise, and the resulting mixture was stirred at 80 °C for 2 h. The resulting solution was extracted with ether. The combined organic layer was washed with brine, and the solvent was removed in vacuo. Purification of the residue by flash column chromatography [hexane−ethyl acetate (2:1)] afforded **39** (1 mg, 13%) as a colorless oil.

Synthesis of (6*R*,8*S*)-1-Acetyl-5-[(triphenylmethoxy)-methyl]-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (40). A solution of **36** (10 mg, 0.02 mmol) in dry THF was treated with NaH (60%, 5 mg, 0.125 mmol) and 18-crown-6 (9.3 mg, 0.035 mmol). The resulting mixture was cooled to 0 °C, acetyl chloride (0.003 mL, 0.04 mmol) was added dropwise, and the reaction mixture was stirred overnight at rt. Brine was added, and the resulting solution was extracted with CH_2Cl_2. The solvent was removed in vacuo. Purification of the residue by flash column chromatography [hexane−ethyl acetate (8:1)] afforded **40** (10 mg, 92%) as a colorless oil: HR FABMS calcd for $C_{35}H_{33}O_2N$ 499.2511, found 499.2520; FABMS *m*/*z* (rel intensity) 499 (M^+, 5), 243 (base); IR ν_{max} ($CHCl_3$) cm^{-1} 3620; ^{1}H NMR ($CDCl_3$) δ 7.74 (1 H, s), 7.59−7.52 (6 H, m), 7.36−7.21 (10 H, m), 6.71 (1 H, d, J = 3.6 Hz), 4.25 (1 H, s), 4.23−4.10 (1 H, m), 3.17−3.11 (1 H, m), 2.64 (3 H, s), 1.83−1.86 (1 H, m), 1.73−1.64 (1 H, m), 1.44−1.23 (1 H, m), 1.17 (3 H, d, J = 7.3 Hz), 1.00 (3 H, d, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 167.21, 144.24, 135.46, 131.35, 131.10, 128.78, 127.81, 126.99, 125.75, 118.68, 109.64, 87.07, 63.54, 40.93, 40.08, 37.83, 24.56, 23.40, 14.08; $[\alpha]^{28}_D$ +121 (*c* 2.7, $CHCl_3$).

Synthesis of (6*R*,8*S*)-1-Acetyl-5-(hydroxymethyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (41). A solution of **40** (14 mg, 0.03 mmol) in methanol and THF (1:1, 1 mL) was treated with 10-camphorsulfonic acid (10 mg, 0.02 mmol). The reaction mixture was stirred for 5 h at rt. Saturated $NaHCO_3$ solution was added, and the resulting solution was extracted with CH_2Cl_2. The combined organic layer was washed with brine, and the solvent was removed in vacuo. Purification of the residue by flash column chromatography [hexane−ethyl acetate (2:1)] afforded **41** (6 mg, 83%) as a colorless oil: HR FABMS calcd for $C_{16}H_{19}O_2N$ 257.1416, found 257.1418; FABMS *m*/*z* (rel intensity) 258 (M + H^+, base), 257 (65); IR ν_{max} ($CHCl_3$) cm^{-1} 3620; ^{1}H NMR ($CDCl_3$) δ 7.50 (1 H, s), 7.35 (1 H, d, J = 4.0 Hz), 6.63 (1 H, d, J = 3.6 Hz), 4.87 (1 H, dd, J = 5.0, 13.5 Hz), 1.34 (1 H, dd, J = 5.3, 13.5 Hz), 4.24−4.19 (1 H, m), 3.51−3.44 (1 H, m), 2.65 (3 H, s), 2.73−2.62 (1 H, m), 1.61 (1 H, s), 1.53 (1 H, dt, J = 1.3, 12.9 Hz), 1.34 (3 H, d, J = 7.3 Hz), 1.21 (3 H, d, J = 7.3 Hz); $[\alpha]^{28}_D$ +124.2 (*c* 1.4, $CHCl_3$).

Synthesis of (6*R*,8*S*)-1-Acetyl-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[*g*]indole-5-carboxaldehyde (42). A solution of **41** (38 mg, 0.15 mmol) in CH_2Cl_2 (8 mL) was treated with active MnO_2 (640 mg, 7.4 mmol). The reaction mixture was stirred at rt for 10 h. The resulting mixture was filtered, and the solvent was removed in vacuo. Purification of the

residue by flash column chromatography [hexane−ethyl acetate (4:1)] afforded **42** (32 mg, 85%) as a colorless oil: HR FABMS calcd for $C_{16}H_{17}O_2N$ 255.1259, found 255.1259; FABMS *m*/*z* (rel intensity) 256 (M + H^+, base), 255 (M^+, 90); IR ν_{max} ($CHCl_3$) cm^{-1} 1715, 1670; ^1H NMR ($CDCl_3$) δ 10.23 (1 H, s), 7.95 (1 H, s), 7.45 (1 H, d, J = 3.6 Hz), 6.75 (1 H, d, J = 4.0 Hz), 4.26−4.15 (1 H, m), 4.05−3.94 (1 H, m), 2.70 (3 H, s), 2.79−2.67 (1 H, m), 1.61 (1 H, dd, J = 1.0, 11.9 Hz), 1.35 (3 H, d, J = 7.0 Hz), 1.19 (3 H, d, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 191.70, 167.33, 149.01, 136.75, 135.05, 131.04, 128.76, 127.09, 123.95, 109.78, 40.48, 39.49, 37.67, 25.54, 24.58, 24.14; $[\alpha]^{24}_D$ +212.8 (*c* 3.0, $CHCl_3$).

Synthesis of (6*R*,8*S*)-6,8-Dimethyl-1-acetyl-α-propyl-1,6,7,8-tetrahydrocyclopent[*g*]indole-5-methanol (43). A solution of PrMgBr (2 mol/L solution in THF, 0.24 mL) was added dropwise to a solution of **42** (57 mg, 0.22 mmol) in dry THF (8 mL) at −10 °C. The reaction mixture was stirred at −10 °C for 30 min. The resulting solution was quenched with a few drops of saturated NH_4Cl solution. Brine was added, and the resulting solution was extracted with CH_2Cl_2. The solvent was removed in vacuo. Purification of the residue by flash column chromatography [hexane−ethyl acetate (2:1)] afforded **43** (43 mg, 64%) as a colorless oil: HR FABMS calcd for $C_{19}H_{25}O_2N$ 299.1885, found 299.1888; FABMS *m*/*z* (rel intensity) 299 (M^+, 84), 282 (base), 256 (51); IR ν_{max} ($CHCl_3$) cm^{-1} 3620; ^1H NMR ($CDCl_3$) δ 7.58 (1 H, s), 7.35 (1 H, d, J = 3.6 Hz), 6.63 (1 H, d, J = 3.6 Hz), 5.04−5.00 (1 H, m), 4.25−4.19 (1 H, m), 3.46−3.41 (1 H, m), 2.65 (3 H, s), 2.69−2.61 (1 H, m), 1.83−1.73 (1 H, m), 1.71−1.63 (1 H, m), 1.61 (1 H, s), 1.55 (1 H, dt, J = 1.0, 11.9 Hz), 1.38 (3 H, d, J = 7.0 Hz), 1.34−1.24 (1 H, m), 1.19 (3 H, d, J = 7.3 Hz), 0.91 (3 H, t, J = 7.4 Hz), 1.03−0.96 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 167.21, 144.03, 137.47, 135.28, 131.55, 126.12, 125.98, 116.40, 109.58, 70.51, 41.66, 40.68, 40.02, 37.83, 24.78, 24.49, 24.24, 19.20, 13.98; $[\alpha]^{28}_D$ +273.2 (*c* 0.9, $CHCl_3$).

Synthesis of (6*R*,8*S*)-5-[(*E*)-1-Butenyl]-6,8-dimethyl-1-acetyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (44). A solution of **43** (10 mg, 0.033 mmol) in dry benzene (2 mL) was treated with *p*-toluenesulfonic acid monohydrate (0.5 mg, 0.003 mmol). The reaction mixture was stirred for 2 h at 50 °C. Saturated $NaHCO_3$ solution was added, and the resulting solution was extracted with CH_2Cl_2. The combined organic layer was washed with brine, and the solvent was removed in vacuo. Purification of the residue by flash column chromatography [hexane−ethyl acetate (2:1)] afforded **44** (8.8 mg, 93%) as a white powder: mp 83 °C; HR FABMS calcd for $C_{19}H_{23}ON$ 281.1780, found 281.1777; FABMS *m*/*z* (rel intensity) 282 (M + H^+, 66), 281 (M^+, base), 266 (16), 238 (14); IR ν_{max} ($CHCl_3$) cm^{-1} 3620; ^1H NMR ($CDCl_3$) δ 7.52 (1 H, s), 7.31 (1 H, d, J = 3.6 Hz), 6.60 (1 H, d, J = 4.0 Hz), 6.56 (1 H, d, J = 1.3 Hz), 6.24 (1 H, dt, J = 6.6, 15.8 Hz), 4.26−4.15 (1 H, m), 3.55−3.33 (1 H, m), 2.63 (3 H, s), 2.72−2.60 (1 H, m), 2.33−2.21 (2 H, m), 1.31 (3 H, d, J = 7.3 Hz), 1.19 (3 H, d, J = 7.3 Hz), 1.11 (3 H, t, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 167.05, 144.50, 135.27, 132.51, 131.33, 131.16, 130.94, 126.83, 126.20, 115.76, 109.55, 40.24, 40.20, 26.26, 24.53, 24.50, 13.80; $[\alpha]^{28}_D$ +334.7 (*c* 0.8, $CHCl_3$).

Synthesis of *cis*-Trikentrin B (1). A solution of **44** (8.8 mg, 0.03 mmol) in dry methanol (1 mL) was treated with sodium borohydride (6 mg, 0.16 mmol). The reaction mixture was stirred for 2 h at rt. Brine was added, and the resulting solution was extracted with CH_2Cl_2. The solvent was removed in vacuo. Purification of the residue by flash column chromatography [hexane−ethyl acetate (10:1)] afforded **1** (7 mg, 93%) as a colorless oil which darkened on standing: HR FABMS calcd for $C_{17}H_{21}N$ 239.1674, found 239.1672; FABMS *m*/*z* (rel intensity) 240 (M + H^+, 90), 239 (M^+, 65), 224 (base); IR ν_{max} ($CHCl_3$) cm^{-1} 3620; ^1H NMR ($CDCl_3$) δ 7.92 (1 H, brs), 7.60 (1 H, s), 7.13 (1 H, dd, J = 2.31, 3.3 Hz), 6.59 (1 H, dm, J = 16.2 Hz), 6.52 (1 H, dd, J = 2.0, 3.3 Hz), 6.17 (1 H, dt, J = 6.6, 15.5 Hz), 3.49−3.46 (2 H, m), 2.70 (1 H, ddd, J = 9.1, 9.1, 13.2 Hz), 2.28−2.23 (2 H, m), 1.54 (1 H, ddd, J = 2.5, 2.5, 13.2 Hz), 1.44 (3 H, d, J = 7.0 Hz), 1.34 (3 H, d, J = 7.3 Hz), 1.11 (3 H, t, J = 7.3 Hz); $[\alpha]^{28}_D$ +100.2 (*c* 0.5, $CHCl_3$).

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Supporting Information Available: Copies of NMR spectra (54 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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