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SYNTHESES OF (±)- AND (–)-CIS-TRIKENTRIN A, (±)- AND (–)-TRANS-TRIKENTRIN A, (±)-CIS-TRIKENTRIN B, (±)-TRANS-TRIKENTRIN B, AND (±)-ISO-TRANS-TRIKENTRIN B

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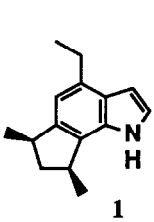
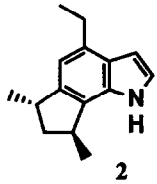
Abstract — Synthesis of the titled indole alkaloids from a marine source was accomplished according to the general scheme in Chart 1. The key steps were preparation of suitably substituted β-hydroxyl carbonyl compounds (**8b**) from **7b**, and the subsequent indole cyclization reaction of **8b** to form **9b**.

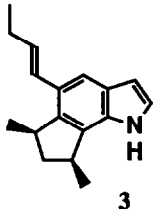
Indole derivatives, cis-trikentrin A (**1**), trans-trikentrin A (**2**), cis-trikentrin B (**3**), trans-trikentrin B (**4**), and iso-trans-trikentrin B (**5**) are constituents of an extract of marine sponge *Trikentrion flabelliforme*, and exhibit a growth inhibitory activity against gram positive bacteria.[1] These natural products are characteristic of the chemical structures of polyalkylindoles, whose substituents are located at the benzene portion of the indole nucleus. Total synthesis of (±)-**1** and (±)-**3** has been reported by MacLeod and Kanematsu, respectively,[2,3] and the absolute structures of **1** and **2** have been clarified by us by a synthesis of their unnatural enantiomers.[4] Here we report our studies of the facile total synthesis of all of the above trikentrins (**1** – **5**) in several steps starting from pyrrole.



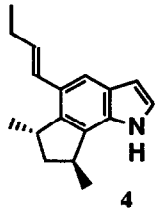
1
cis-trikentrin A



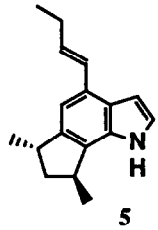
2
trans-trikentrin A



3
cis-trikentrin B

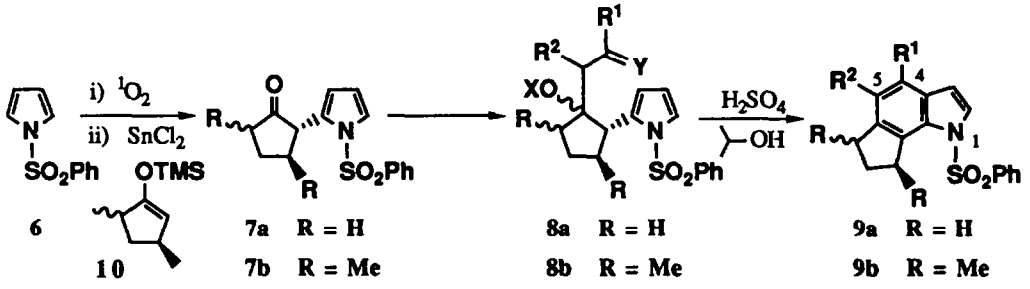


4
trans-trikentrin B



5
iso-trans-trikentrin B

Our synthesis pathway consisted mainly of three operations (Chart 1): (i) the sensitized photooxygenation of phenylsulfonylpyrrole (**6**), followed by nucleophilic addition of 1-(trimethylsilyloxy)cyclopentene in the presence of tin (II) chloride to give the 2-pyrrolylcyclopentanone derivative (**7**);[5] (ii) elongation of the necessary carbon side chain to form β-hydroxyl ketone or aldehyde compound (**8**); and (iii) the sulfuric acid-catalyzed indole cyclization reaction[6] of **8** to yield 1-phenylsulfonyl-1,6,7,8-tetrahydrocyclopent[*g*]indole derivative (**9**). Our preliminary experiment utilizing **7a** revealed that the condensation of the carbonyl side chain with the ketone group of **7a** was effected by the Mukaiyama reaction,[7] the Corey and Enders procedure,[8] and the Wittig directed aldol condensation reaction.[9] Thus two indole compounds (**9a**), *i.e.*, a 4-ethyl derivative (R^1 = Et, R^2 = H) and a 5-butyl derivative (R^1 = H, R^2 = n-Bu) have been synthesized as models for trikentrins A and B.[10]



R^1, R^2 = H, Alkyl side chain X = H or Alkyl group Y = Carbonyl or its equivalent

Chart 1

Synthesis of (±)-cis-Trikentrin A and (±)-trans-Trikentrin A

Natural products synthesis was started by preparing the common material (**7b**) leading to the five trikentrins. 2,4-Dimethylcyclopentanone,[11] whose ratio of cis- and trans-dimethyl components was determined to be *ca.* 2:1 by inspection of ^{1}H- and ^{13}C-nmr spectra,[12] was converted to 3,5-dimethyl-1-(trimethylsilyloxy)cyclopentene (**10**) by Corey's protocol.[13] This was coupled with **6** according to the previously reported procedure[5,10] to afford the required **7b** in 55% yield, calculated from **6**, as a mixture of two diastereomeric isomers (cis : trans = 5 : 2). The trans nature of the 2-pyrrolyl function against the neighboring methyl group on the cyclopentanone ring was deduced from the stereochemical course of the condensation reaction as illustrated by **11** in Chart 2.

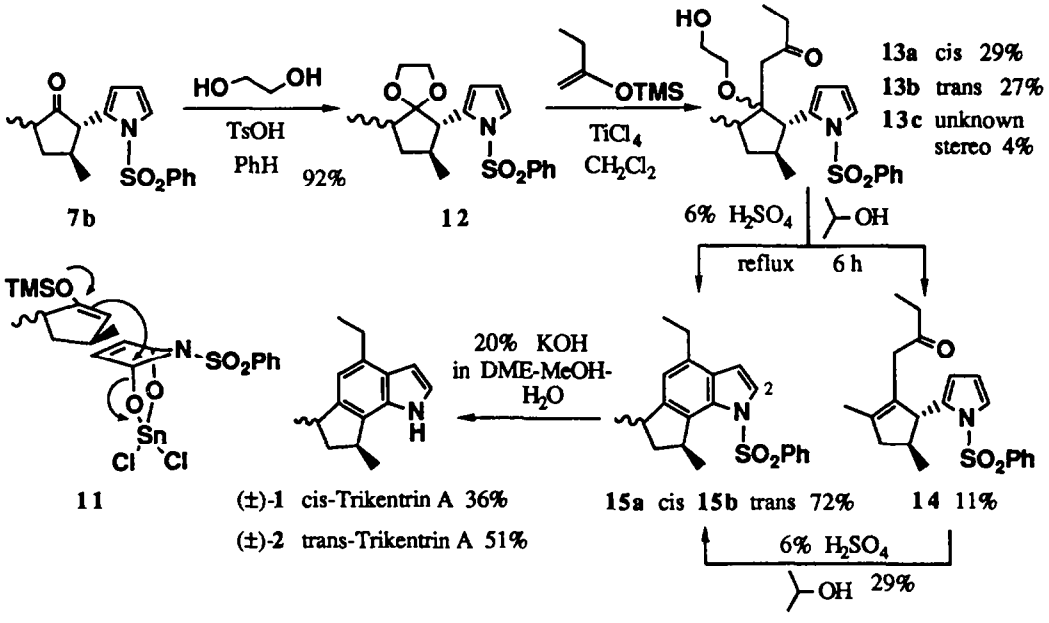


Chart 2

The cyclopentanone derivative (**7b**) was transformed to its ethylene acetal (**12**) in the usual manner,[15] and this was submitted to the reaction[7] with 2-(trimethylsilyloxy)-1-butene in the presence of titanium (IV) chloride in dichloromethane at about -40°C. After separation over silica gel, the expected products (**13a** and **13b**) having cis- and trans-dimethyl configuration were obtained in 29% and 27% yields, respectively, accompanied by the product (**13c**) with unknown stereochemistry in 4% yield, along with the recovery of the starting material in the form of the ethylene acetal compound (**12**, 22%) and the ketone derivative (**7b**, 6%). The three products (**13a**, **13b**, and **13c**) were combined and subjected to the indole cyclization reaction[6,10] using 6% H_2SO_4 in 2-propanol at reflux for 6 h. An inseparable mixture of the desired indole compounds (**15a** and **15b**) in the ratio of 4 : 5 was produced in 72% yield, accompanied by the formation of **14** in 11% yield. Indole cyclization from the latter proceeded rather sluggishly, and the additional mixture of **15a** and **15b** was obtained in only 29% yield after refluxing with 6% H_2SO_4 in 2-propanol for 14 h. All the mixture of **15a** and **15b** was then treated with 20% potassium hydroxide in dimethoxyethane-methanol-water (1:1:1) at 85 - 90°C for 6 h. Careful separation by repeated preparative thin-layer chromatography afforded (±)-cis-trikentrin A (**1**) and (±)-trans-trikentrin A (**2**) in 36% and 51% yields, respectively, as colorless syrups, which became solid in the refrigerator and turned purple on prolonged storage. The synthetic materials were identified as the natural products by comparison of their ^{1}H- and ^{13}C-nmr spectra.

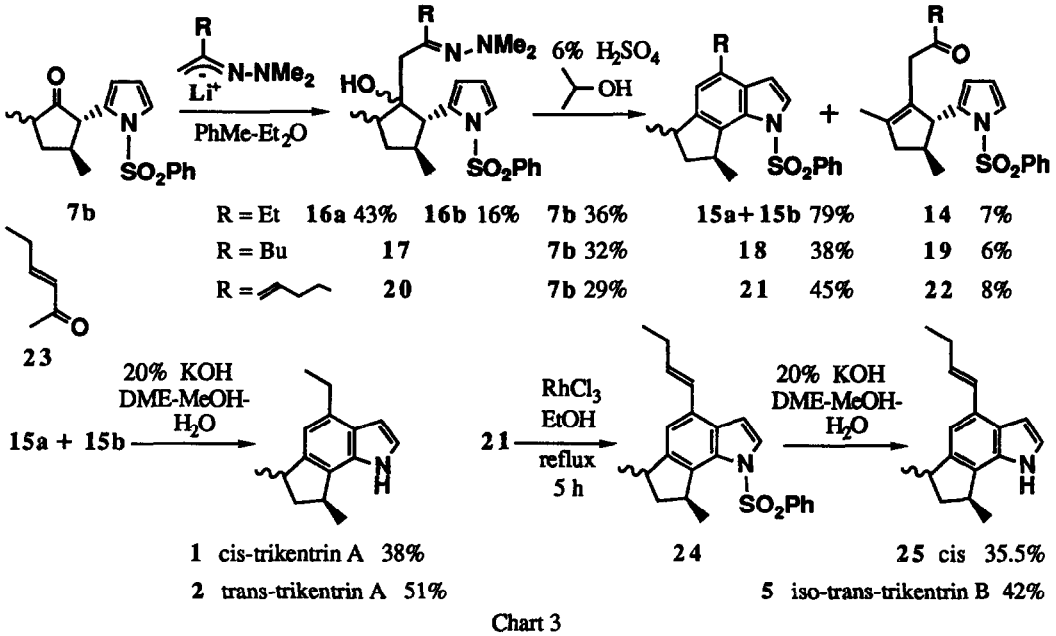


Chart 3

In the separate experiments, both **13a** and **13b** were independently cyclized to the coresponding indole derivatives using the conditions mentioned above, furnishing **15a** and **15b** in a pure state in 71% and 75% yields, which were hydrolyzed as above with alkali to afford (±)-**1** and (±)-**2** in 83% yield each. Thus the stereochemical relationship between two dimethyl groups in **13a**, **13b**, **15a**, and **15b** became evident. In the ^{1}H-nmr spectra of

15a and **15b**, the doublet proton signals of the C-2 position were visible at 7.46 ppm and 7.59 ppm, respectively, and these signals were useful for determining the ratio of the inseparable mixture of **15a** and **15b**.

An alternative shorter pathway was examined next (Chart 3). To elongate an appropriate carbon side chain from the ketone group of **7b**, organometallic reagents are proper choices we must consider. However, the ketone compound (**7b**) bearing dimethyl groups is more sterically congested and far more readily enolizable than **7a**. The Grignard reaction proceeded only in a poor yield with the recovery of most of the starting material (**7b**). Therefore, the reaction [8] of the lithium salt of 2-butanone *N*, *N*-dimethylhydrazone[16] with **7b** was studied using a variety of solvent systems of different polarities. A mixture of toluene and diethyl ether (1 : 1) afforded the best result even with the recovery of **7b** in 36% yield, providing two isomers (**16a** and **16b**) in 43% and 16% yields, whose stereochemistry was not investigated. It was delightful to find that the dimethylhydrazone (**16a** and **16b**) behaved the same as the ketone derivatives (**13**) towards the H_2SO_4-catalyzed indole cyclization reaction. The combined **16a** and **16b** was directly refluxed in 6% H_2SO_4-containing 2-propanol for 8 h to form **15a** and **15b** (3 : 4) in 79% yield, accompanied by the formation of **14** in 7% yield. A mixture of **15a** and **15b** was finally hydrolyzed with alkali as above, and (±)-cis-trikentrin A (**1**) and (±)-trans-trikentrin A (**2**) were obtained in 38% and 51% yields, respectively. Thus the natural product was synthesized in four steps from 1-phenylsulfonylpyrrole (**6**).

Synthesis of (±)-Iso-trans-trikentrin B

As a natural consequence of the above result, 3-hexen-2-one (**23**) is a suitable carbon unit for the synthesis of iso-trans-trikentrin B (**5**) (Chart 3). However, *N*, *N*-dimethylhydrazone of this enone (**23**) is hardly accessible due to the inevitable addition of the second molecule of *N*, *N*-dimethylhydrazine in the Michael manner to the conjugated double bond.[8] Preparation of the trimethylsilyl enol ether of **23** was possible, but the reaction of this with **12** in the presence of titanium (IV) chloride afforded only an uncharacterized compound. Therefore our initial plan for the synthesis of iso-trans-trikentrin B was to acquire the correspoding saturated compound (**18**) and functionalize the butyl side chain to introduce the double bond at the required position. Employing the above-mentioned result, preparation of **18** was straightforward. The ketone derivative (**7b**) was treated with the lithium salt of 2-hexanone *N*, *N*-dimethylhydrazone, the reaction products were roughly separated to remove the recoved **7b** (32% yield), and the combined isomers (**17**) were subjected to the indole cyclization reaction for 8 h to afford **18** and **19** in 38% and 6% yields, calculated from **7b**. But several attempts to oxidize the benzylic position of the butyl side chain of **18** were unsuccessful.

A satisfactory result was obtained by first placing the double bond at a position remote from the carbonyl group; after the indole formation, it was shifted to the conjugate position with the aromatic ring. The phenylsulfonyl group functioned strongly to protect the indole ring against the rather drastic conditions for migration of the double bond. Thus commercial 5-hexen-2-one was converted to its *N*, *N*-dimethylhydrazone. This was used to treat **7b** as usual and the resulting mixture of **20** was cyclized to the indole derivative (**21**) in 45% yield by refluxing with 6% H_2SO_4 – 2-propanol for 5.5 h. Migration of the terminal double bond to the required position was effected by refluxing an ethanol solution of **21** with a catalytic amount of rhodium (III) chloride for 5 h.[17] A crude mixture of **24**, obtained in *ca.* 95% yield, was then hydrolyzed with alkali and repeated preparative thin-layer chromatography afforded (±)-iso-trans-trikentrin B (**5**) in 42% yield, together with the corresponding cis derivative (**25**) in 35.5% yield, calculated from **21**. The synthetic material was identified as the natural product by comparing their ^{1}H- and ^{13}C-nmr spectra.

Synthesis of (±)-cis-Trikentrin B and (±)-trans-Trikentrins B

Preliminary experiments indicated that the aldehyde *N*, *N*-dimethylhydrazone was unsuitable for the synthesis of trikentrins B, because a side reaction occurred predominantly in the condesation process with **7a**.[10] Therefore the Wittig's method[9] was applied to **7b** and the reaction with the lithium salt of hexanal *N*-cyclohexyl-imine[18] was tried first in a solution of tetrahydrofuran and toluene (5:1) at -77 – -62°C for 1 h (Chart 4). Thin-layer chromatography of the crude reaction products (**26**) showed that a considerable amount of the starting material (**7b**) remained in the mixture, but this was further treated with 6% H_2SO_4 in 2-propanol to give the indole derivative (**27**) (cis:trans = 6:5) in 22.5% yield with the recovery of **7b** in 52% yield. A preliminary experiment[10] also taught us that some unidentified materials generated from an imine such as **26** resisted the indole formation reaction, but the correspoding aldehyde derivative produced an indole derivative quite readily. Therefore the following modification was adopted for the natural product synthesis: (i) a solvent system of *ca.* a 1:1 mixture of toluene and diethyl ether should be used; and (ii) the hydrolysis operation was introduced to substantiate the aldehyde derivatives (**29**) just after the carbanion reaction.

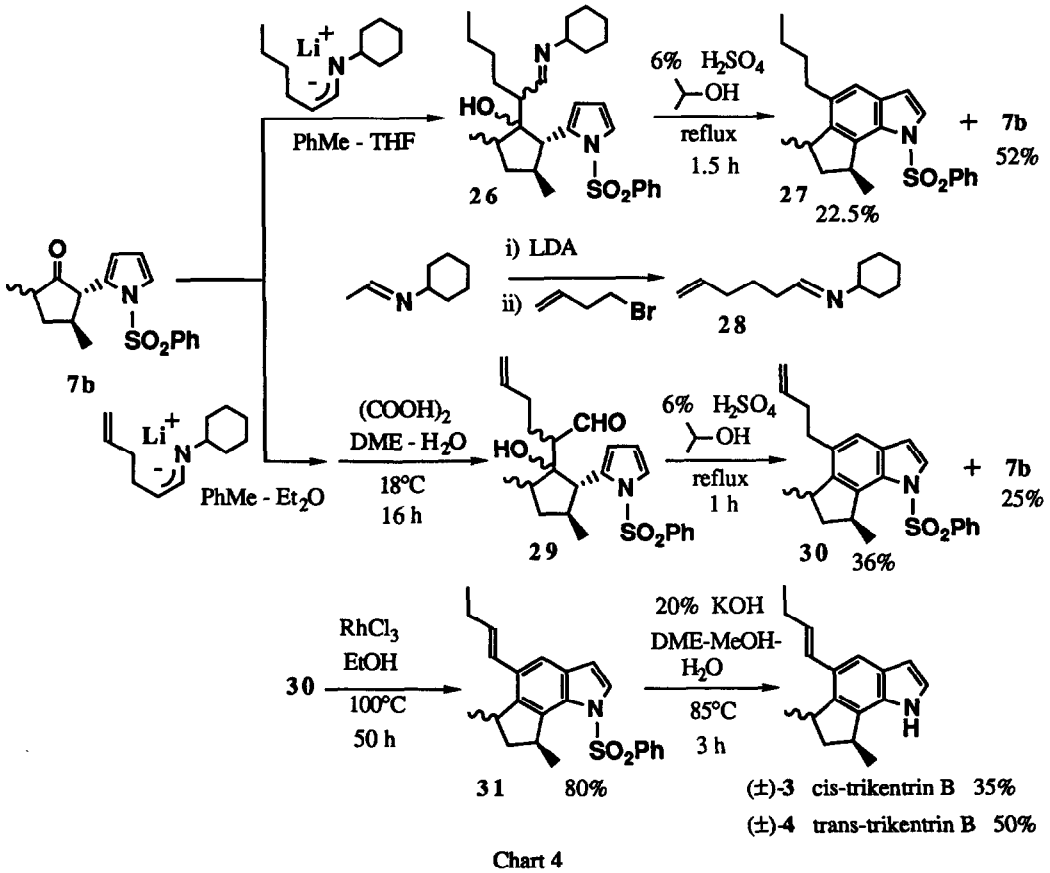


Chart 4

The necessary reagent (**28**) was prepared from acetaldehyde *N*-cyclohexylimine as shown in Chart 4 and it was condensed with **7b** as above in toluene-diethyl ether. The mixture of the reaction products was treated with oxalic acid[19] in a solution of dimethoxyethane and water, and then the crude aldehyde derivatives (**29**) obtained were cyclized to the desired indole compound (**30**) (cis/trans = 1.4) in 36% yield calculated from **7b**, with the recovery of **7b** in 25% yield. In contrast to the ready migration of the double bond in the iso-trans-trikentrin B synthesis, conversion of **30** into **31** required an enforced condition, and **31** was produced in 80% yield after heating an ethanol solution of **30** with rhodium (III) chloride in a sealed tube at 100°C for 50 h. Alkaline hydrolysis of **31** afforded (±)-cis-trikentrin B (**3**) and (±)-trans-trikentrin B (**4**) in 50% and 35% yields, respec-tively; their identity with the natural compounds was confirmed by comparing their ^{1}H- and ^{13}C-nmr spectra.

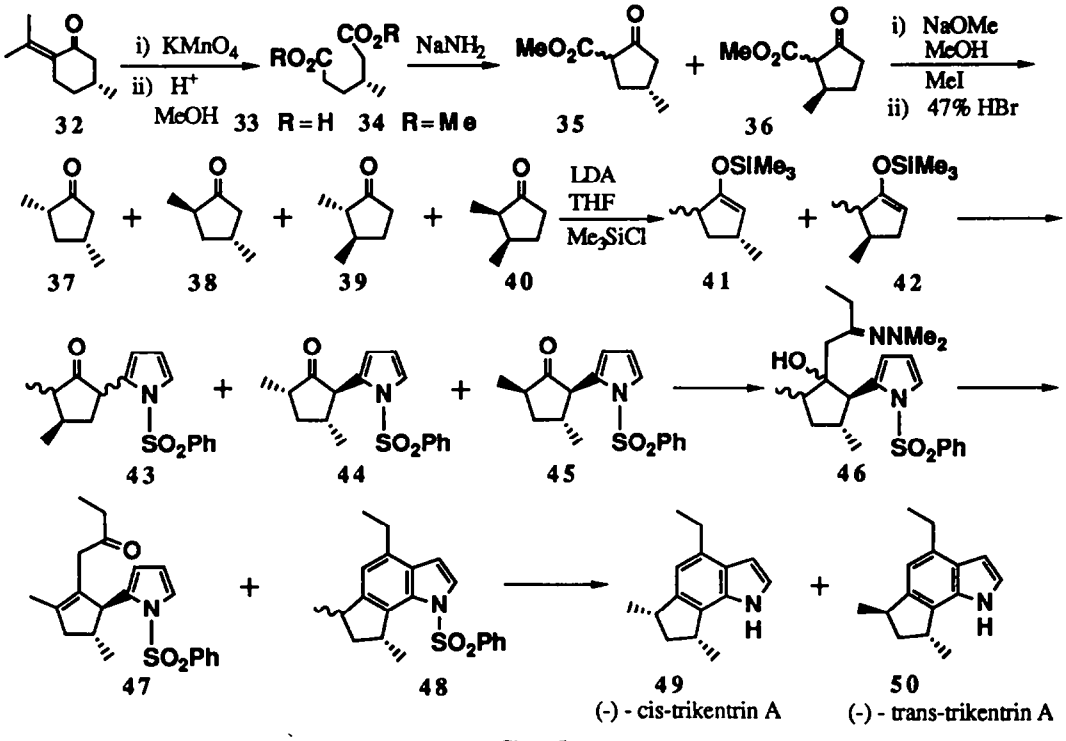


Chart 5

Determination of the Absolute Configuration of cis- and trans-Trikentrins A by Synthesis of Their Enantiomers[20]

A chiral synthesis of trikentrins A was started from (4*R*)-methyl 4-methylcyclopentan-2-onecarboxylate (**35**),[21] reported to be readily prepared from commercially available (*R*)-(+)-pulegone (**32**) by way of (*R*)-3-methyladipic acid (**33**) and its dimethyl ester (**34**) (Chart 5). Contrary to the description in the literature[21] that the Dieckmann condensation reaction of **34** using sodium amide afforded solely **35**, a considerable amount of **36** was included in the condensation product (**35**). This was made clear by the fact that the sodium methoxide-catalyzed methylation of the Dieckmann products, and successive removal of the methyl carboxylate group with concetrated hydrobromic

acid gave in 71% yield a mixture of dimethylcyclopentanones having the structures of **37**, **38**, **39**, and **40** in the ratio of *ca.* 2 : 1 : 1.3 : 0.1, which was estimated from the integrated values of the methyl signals in the ^{1}H-nmr spectrum of the mixture. The methyl proton signals of **37** and **38** were assigned by comparing their chemical shifts with those of racemic 2,4-dimethylcyclopentanone that was used as one of the starting compounds for the synthesis of racemic trikentrins A. The methyl proton signals of **39** and **40** were verified by the chemical shift data reported in the literature.[22]

The above mixture of dimethylcyclopentanones (**37** – **40**) was then trimethylsilylated[13] to give a mixture of **41** and **42** in 90% yield and these were coupled with phenylsulfonylpyrrole (**6**) as shown in Chart 1. Separation over silica gel afforded two groups of mixtures in 37% and 19% yields, respectively, which consisted of a mixture of the necessary isomers of **44** and **45** (4 : 1) in one part and an unwanted mixture of the possible four isomers (**43**) in another. The former mixture (**44** and **45**) was further treated with the lithium salt of 2-butanone *N*, *N*-dimethylhydrazone, and **46** was obtained in 61% yield, accompanied by the recovery of **44** and **45** in the ratio of *ca.* 11 : 1 in 32% yield. Indole cyclization was carried out as usual by refluxing **46** in 6.5% sulfuric acid – 2-propanol for 14 h to give **48** (cis : trans = 4 : 3) in 73% yield along with the by-product (**47**) in 12% yield. Alkaline hydrolysis of **48**, followed by separation over silica gel afforded (-)-cis-trikentrin A (**49**) and (-)-trans-trikentrin A (**50**) in 52% and 37% yields, which were identical with **1** and **2** (^{1}H- and ^{13}C-nmr spectra) except for the opposite sign of the optical rotation. Therefore this study concludes that the absolute structures of the natural cis- and trans-trikentrins A can be depicted as **1** and **2**, and furthermore those of other trikentrins are assumed to be **3**, **4**, and **5**.

EXPERIMENTAL

Melting points (mp) were determind on Yanagimoto micro-melting point apparatus and are not corrected. Optical rotations were measured on JASCO DIP-370 Digital Polarimeter. Mass spectra (MS) were taken on Hitachi RMS-4 spectrometer. High resolution mass spectra (HRMS) were measured on JEOL JMS-DX-300 spectrometer. Infrared absorption spectra (IR) were determined on Hitachi 215 spectrophotometer. Proton magnetic resonance (^{1}H NMR) spectra were recorded on Varian EM 390 spectrometer unless otherwise specified. 400MHz ^{1}H NMR and 100 MHz ^{13}C NMR spectra were recorded on JEOL JMN-GX-400. Column chromatography was conducted on silica gel, Fuji Davison BW 200, and preparative thin-layer chromatography (PTLC) was carried out on glass plates (20 × 20 cm) coated with Merck silica gel 60 PF_{254} (1 mm thick).Usual work-up refers to washing the organic layers with water or brine, drying over anhydrous sodium sulfate and evaporating the solvents under reduced pressure.

3,5-Dimethyl-1-(trimethylsilyloxy)cyclopentene (10) — A stirred solution of LDA, prepared from diisopropylamine (9.0 ml) and 15% BuLi - hexane (39.5 ml) in THF (70 ml) under Ar atmosphere at -20°C for 20 min, was cooled to -75°C, and to this was added dropwise chlorotrimethylsilane (27.0 ml) and then a THF (20 ml) solution of 2,4-dimethylcyclopentanone (cis/trans = *ca.* 2, 6.00 g) during 7 min. After being stirred at -80 – -68°C for 10 min, Et_3N (37.0 ml) was added dropwise in 5 min and the mixture was stirred at -75 – -68°C for 5 min. It was poured into sat. $NaHCO_3$-H_2O and the mixture was extracted with hexane. The organic layer was successively washed with H_2O, 0.1 *N* citric acid, sat. $NaHCO_3$-H_2O, and H_2O; and usual work-up and distillation afforded **10** (8.40 g, 85%), colorless oil, bp 72 – 76°C/47 mmHg. ^{1}H NMR ($CDCl_3$) δ: 0.19 (9H, s), 4.50 (1H, br s).

3,5-Dimethyl-2-(1-phenylsulfonyl-2-pyrrolyl)cyclopentanone (7b) — According to the reported procedure,[5,10] a solution of 1-phenylsulfonylpyrrole (**6**) (1.507 g) and methylene blue (50 mg) in CH_2Cl_2 (120 ml) was photooxygenated at -65 – -70°C for 5 h. To this was added successively a CH_2Cl_2 (10 ml) solution of **10** (1.674 g), and an EtOAc (50 ml) solution of $SnCl_2$ (1.724 g) during 15 min, and the mixture was stirred at *ca.* -75°C for 1 h, and then at 0°C for 2 h to yield a residue (2.9 g) after the reported work-up. Purification by column chromatagraphy [hexane-CH_2Cl_2 (1:1)] afforded the recovery of **6** (146 mg, 10%) and **7b** (1.263 g, 55%), colorless syrup (cis:trans = 5:2). MS *m/z*: 317 (M^+). IR ($CHCl_3$) cm^{-1}: 1742. ^1H NMR ($CDCl_3$) δ: 0.92 and 0.95 (3H, 5:2, d each, J=6 Hz), 1.08 (3H, d, J=6 Hz), 3.53 and 3.76 (1H, 5:2, d each, J=11 Hz), 5.89 and 5.96 (1H, 2:5, dd each, J=3, 1.5 Hz), 6.21 and 6.23 (1H, 5:2, dd each, J=3, 3 Hz), 7.20 and 7.27 (1H, 5:2, dd each, J=3, 1.5 Hz), 7.33-7.68 (3H, m), 7.68-7.94 (2H, m). This was partially crystallized and repeated recrystallization from MeOH-H_2O gave the pure cis isomer, colorless prisms, mp 86.5 – 87.5°C. Anal. Calcd for $C_{17}H_{19}NO_3S$: C, 64.33; H, 6.03; N, 4.41. Found: C, 64.35; H, 5.95; N, 4.33. IR (KBr) cm^{-1}: 1736.

3,5-Dimethyl-2-(1-phenylsulfonyl-2-pyrrolyl)cyclopentanone Ethylene Acetal (12) — A benzene (20 ml) solution of **7b** (232 mg), ethylene glycol (1.0 ml) and *p*-TsOH·H_2O (15 mg) was refuxed for 21 h using Dean-Stark apparatus. After cooling, sat. $NaHCO_3$-H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and PTLC [hexane-EtOAc (6:1)] afforded **12** (243 mg, 92%), colorless syrup. MS *m/z*:361 (M^+). ^1H NMR ($CDCl_3$) δ: 0.56 and 0.63 (3H, d each, J=6 Hz), 0.85 and 0.92 (3H, d each, J=6 Hz), 6.15 (1H, dd, J=3.5, 2 Hz), 6.24 (1H, dd, J=3.5, 3.5 Hz), 7.33 (1H, dd, J=3.5, 2 Hz), 7.23-7.62 (3H, m), 7.62-7.90 (2H, m).

2-(Trimethylsilyloxy)-1-butene — Empolying the Corey's procedure[13] as above, 2-butanone (4.99 g) was treated with LDA, prepared from diisopropylamine (10.30 ml) and 15% BuLi-hexane (46.7 ml) in THF (80 ml), and chlorotrimethylsilane (18.10 ml) at -70 – -60°C for 15 min. Et_3N (20.3 ml) was added to this and the mixture was stirred at -70°C for 5 min. This was poured into sat. $NaHCO_3$-H_2O, the mixture was shaken with Et_2O, the organic layer was worked up as above, and distillation of the residue afforded 2-(trimethylsilyloxy)-1-butene (4.03 g, 40%) as colorless oil, bp 107 – 113°C. IR (neat) cm^{-1}: 1628. ^1H NMR ($CDCl_3$) δ: 0.29 (9H, s), 1.08 (3H, t, J=7.5 Hz), 2.08 (2H, q, J=7.5 Hz), 4.07 (2H, s).

Titanium (IV) Chloride-Catalyzed Reaction of 12 with 2-(Trimethylsilyloxy)-1-butene — A CH_2Cl_2 (3.5 ml) solution of **12** (50 mg) and 2-(trimethylsilyloxy)-1-butene (102 mg) was treated with $TiCl_4$ (46 μl) under Ar atmosphere at -47 – -35°C for 1.25 h. The reaction was quenched with sat. $NaHCO_3$-H_2O, the mixture was extracted with CH_2Cl_2 and the CH_2Cl_2 layer was worked up as usual. PTLC [hexane-EtOAC (5:1)] afforded three products, **13b** (16 mg, 27%), **13a** (17.5 mg, 29%), and **13c** (2.5 mg, 4%) in the order of the increasing polarity, accompanied by the recovered **12** (11 mg, 22%) and **7b** (2.5 mg, 6%, cis/trans = *ca.* 3.5). **13a**: Colorless syrup. MS *m/z*: 433 (M^+). IR ($CHCl_3$) cm^{-1}: 1712. ^1H NMR ($CDCl_3$) δ: 0.23 (3H, d, J=6 Hz), 0.94 (3H, d, J=6 Hz), 1.00 (3H, t, J=7 Hz), 6.11-6.36 (2H, m). **13b**: Colorless syrup. MS *m/z*: 433 (M^+). IR ($CHCl_3$) cm^{-1}: 1720. ^1H NMR ($CDCl_3$) δ: 0.26 (3H, d, J=7 Hz), 0.93 (3H, d, J=7 Hz), 1.08 (3H, t, J=7 Hz), 6.13-6.34 (2H, m).

6,8-Dimethyl-4-ethyl-1-phenylsulfonyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (15a, 15b) — The three products (**13a**, **13b**, and **13c**) obtained above were combined and treated with 6% H_2SO_4 – 2-propanol (4.5 ml) under reflux for 6 h. The reported work-up[6,10] and PTLC [hexane-EtOAC (12:1)] gave a mixture of **15a** and **15b** (4:5) (21 mg, 72%) and **14** (3.5 mg, 11%). Spectral data of pure **15a** and **15b** are shown below. **14**: Colorless syrup. MS *m/z*: 371 (M^+). IR ($CHCl_3$) cm^{-1}: 1711. ^1H NMR ($CDCl_3$) δ: 0.89 (3H, t, J=7 Hz), 0.89 (3H, d, J=6.5 Hz), 1.64 (3H, s), 2.12 (2H, q, J=7 Hz), 2.58 (1H, d, J=15.5 Hz), 3.00 (1H, d, J=15.5 Hz), 3.64 (1H, br s), 5.74 (1H, dd, J=3.5, 2 Hz), 6.15 (1H, dd, J=3.5, 3.5 Hz), 7.29 (1H, dd, J=3.5, 2 Hz), 7.36-7.62 (3H, m), 7.62-7.85 (2H, m).

Indole Cyclization of the Compound (14) — The same treatment of **14** (5.5 mg) as above with 6% H_2SO_4 – 2-propanol (3 ml) under reflux for 14 h afforded a mixture of **15a** and **15b** (*ca.* 1:1) (1.5 mg, 29%) after PTLC [hexane-EtOAc (9:1)].

(±)-cis-Trikentrin A (1) and (±)-trans-Trikentrin A (2) — A solution of **15a** and **15b** in 10% KOH – DME-MeOH-H_2O (1:1:1) (3 ml) was heated at 85-90°C for 6 h. After coling, sat. NH_4Cl-H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and PTLC [Merck SiO_2 60 F_{254} (20 × 20 cm) plate, three sheets, hexane-CH_2Cl_2 (24:1), six times development] afforded (±)-**1** (4.5 mg, 36%) as a less polar substance and (±)-**2** (6.5 mg, 51%) as a more polar substance. (±)-cis-Trikentrin A (**1**): Unstable colorless oil, which turned purple on standing. HRMS Calcd for $C_{15}H_{19}N$: 213.152. Found: 213.154. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.32 (1H, ddd, J=12, 8.5, 8.5 Hz), 1.36 (3H, dd, J=7.5, 7.5 Hz), 1.37 (3H, d, J=7 Hz), 1.50 (3H, d, J=7 Hz), 2.61 (1H, ddd, J=12, 7.5, 7.5 Hz), 2.91 (1H, dq, J=15, 7.5 Hz), 2.96 (1H, dq, J=15, 7.5 Hz), 3.23 (1H, ddq, J=8.5, 7.5, 7 Hz), 3.44 (1H, ddq, J=8.5, 7.5, 7 Hz), 6.59 (1H, dd, J=3, 2 Hz), 6.84 (1H, s), 7.16 (1H, dd, J=3, 3 Hz), 8.09 (1H, br s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 15.0, 20.8, 21.0, 26.5, 37.2, 38.9, 44.7, 101.4, 114.0, 122.8, 126.3, 127.0, 132.4, 135.0, 143.0. (±)-trans-Trikentrin A (**2**): Unstable colorless oil, which turned purple on standing. HRMS Calcd for $C_{15}H_{19}N$: 213.152. Found: 213.150. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.30 (3H, d, J=7 Hz), 1.33 (3H, d, J=7 Hz), 1.36 (3H, t, J=7.5 Hz), 1.96 (1H, ddd, J=12.5, 7, 7 Hz), 2.05 (1H, ddd, J=12.5, 7, 3.5 Hz), 2.94 (2H, q, J=7.5 Hz), 3.41 (1H, ddq, J=7, 7, 7 Hz), 3.53 (1H, ddq, J=7, 3.5, 7 Hz), 6.60 (1H, dd, J=3, 2 Hz), 6.83 (1H, s), 7.16 (1H, dd, J=3, 3 Hz), 8.02 (1H, br s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 15.0, 20.0, 20.8, 26.5, 36.0, 37.9, 43.8, 101.5, 114.1, 122.8, 126.1, 127.3, 132.1, 135.1, 142.5.

(±)-1-Phenylsulfonyl-cis-trikentrin A (15a) and (±)-1-Phenylsulfonyl-trans-trikentrin A (15b) — The compounds [**13a** (20 mg) and **13b** (20.5 mg)] obtained above were separately heated with 6% H_2SO_4 – 2-propanol (4.5 ml each) for 12 h and 5 h, respectively. The same work-up as above and PTLC [hexane-EtOAc (12:1)] afforded **15a** (11.5 mg, 71%) and **15b** (12.5 mg, 75%). **15a**: Colorless syrup. MS *m/z*: 353 (M^+). ^1H NMR ($CDCl_3$) δ: 1.19 (3H, t, J=7.5 Hz), 1.33 (6H, d, J=7 Hz), *ca.* 1.33-1.56 (1H, m), 2.55 (1H, ddd, J=12.5, 8.5, 8.5 Hz), 2.73 (2H, q, J=7.5 Hz), 3.00-3.44 (1H, m), 3.84-4.26 (1H, m), 6.64 (1H, d, J=4 Hz), 6.89 (1H, s), 7.14-7.74 (5H, m), 7.46 (1H, d, J=4 Hz). **15b**: Colorless syrup. HRMS Calcd for $C_{21}H_{23}NO_2S$: 353.145. Found: 353.145. ^1H NMR ($CDCl_3$) δ: 1.03 (3H, d, J=6.5 Hz), 1.23 (3H, d, J=6.5 Hz), 1.23 (3H, t, J=7.5 Hz), 1.63 (1H, ddd, J=11.5, 10, 7 Hz), 1.97 (1H, dd, J=11.5, 6.5 Hz), 2.79 (2H, q, J=7.5 Hz), 3.30 (1H, ddq, J=10, 6.5, 6.5 Hz), 3.96 (1H, dq, J=7, 6.5 Hz), 6.68 (1H, d, J=4 Hz), 6.88 (1H, s), 7.19-7.56 (3H, m), 7.56-7.79 (2H, m), 7.59 (1H, d, J=4 Hz).

Alkaline Hydrolysis of 15a and 15b — The compounds [**15a** (7 mg) and **15b** (4 mg)] were separately hydrolyzed with 10% KOH – DME-MeOH-H_2O (1:1:1) (1.5 ml each) at reflux for 6 h. The same work-up as above and PTLC [hexane-CH_2Cl_2 (6:1)] gave (±)-cis-trikentrin A (**1**) (3.5 mg, 83%) and (±)-trans-trikentrin A (**2**) (2 mg, 83%).

Preparation of 16a and 16b from 7b — An Et_2O (3 ml) solution of 2-butanone *N*, *N*-dimethylhydrazone (180 mg) was treated with 15% BuLi in hexane (0.81 ml) under Ar atmosphere at -52 – -40°C for 1 h. After cooling at -80°C, a toluene (3 ml) solution of **7b** (50 mg) was added dropwise and the whole was stirred at -80 – -65°C for 1 h. It was quenched with sat. NH_4Cl-H_2O, the mixture was extracted with Et_2O, usual work-up, and PTLC [hexane-EtOAc (4:1)] gave the less polar compound (**16a**) (29 mg, 43%) and the more polar compound (**16b**) (11 mg, 16%), along with the recovery of **7b** (18 mg, 36%, cis/trans = 11). **16a**: Colorless syrup. MS *m/z*: 431 (M^+). IR ($CHCl_3$) cm^{-1}: 1628. ^1H NMR ($CDCl_3$) of the major isomer δ: 0.27 (3H, d, J=6.5 Hz), 0.90 (3H, d, J=6.5 Hz), 1.03 (3H, t, J=7.5 Hz), 2.26 (6H, s), 6.28 (1H, dd, J=3.5 3.5 Hz), 6.41 (1H, dd, J=3.5, 2 Hz). **16b**: Colorless syrup. MS *m/z*: 431 (M^+). IR ($CHCl_3$) cm^{-1}: 1628. ^1H NMR ($CDCl_3$) of the major

isomer δ: 0.33 (3H, d, J=6.5 Hz), 0.99 (3H, d, J=7 Hz), 1.01 (3H, t, J=7 Hz), 2.17 (6H, s), 6.29 (1H, dd, J=3.5, 3.5 Hz), 6.29-6.44 (1H, m).

Alternative Synthesis of (±)-cis-Trikentrin A (1) and (±)-trans-Trikentrin A (2) — The compound [**16a** (29 mg) and **16b** (11 mg)] were combined and treated with 6% H_2SO_4 – 2-propanol (4.5 ml) at reflux for 8 h. The same work-up as above and PTLC [hexane-EtOAc (9:1)] afforded a mixture of **15a** and **15b** (*ca.* 3:4) (26 mg, 79%), and **14** (2.5 mg, 7%). According to the procedure described above, the mixture of **15a** and **15b** (26 mg) was converted to (±)-**1** (6 mg, 38%) and (±)-**2** (8 mg, 51%).

2-Hexanone *N*, *N*-Dimethylhydrazone — According to the literatue,[8] this was prepared in 91% yield as colorless oil, bp 85-88°C/70 mmHg. IR (neat) cm^{-1}: 1640. ^1H NMR ($CDCl_3$) δ: 0.90 (3H, dif t J=7 Hz), 1.10-1.72 (4H, m), 1.93 (3H, s), 2.07-2.31 (2H, m), 2.42 (6H, s).

4-(1-Butyl)-6,8-dimethyl-1-phenylsulfonyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (18) — A toluene (3 ml) solution of **7b** (50 mg) was added dropwise to a cooled (-78°C) solution of the lithium salt of 2-hexanone *N*, *N*-dimethylhydrazone in Et_2O (3 ml), prepared from the hydrazone (224 mg) and 15% BuLi-hexane (0.81 ml) under Ar atmosphere at -54 – -41°C for 1 h. After being stirred at -78 – -63°C for 1 h, the reaction was quenched with sat. NH_4Cl-H_2O and the mixture was extracted with Et_2O. Usual work-up and PTLC [hexane-EtOAc (5:2), and then hexane-CH_2Cl_2 (1:2) for the recovery] afforded crude **17** (45 mg) and **7b** (16mg, 32%, cis/trans = 11). The crude product (**17**) (45 mg) was refluxed in 6% H_2SO_4 – 2-propanol (4.5 ml) for 8 h. The same work-up as above and PTLC [hexane-EtOAc (9:1)] gave **18** (23mg, 38% from **7b**) and **19** (4 mg, 6% from **7b**). **18**: Colorless syrup (cis:trans=*ca.* 2:3). MS *m/z*: 381 (M^+). ^1H NMR ($CDCl_3$) δ: 1.96 (1H of the trans isomer, dd, J=11.5, 6.5 Hz), 2.34-2.88 (1H of the cis isomer and 2H, m), 3.00-3.52 (1H, m), 3.78-4.25 (1H, m), 6.63 and 6.69 (1H, 2:3, d each, J=4 Hz), 6.86 (1H, s). **19**: Colorless syrup. MS *m/z*: 399 (M^+). IR ($CHCl_3$) cm^{-1}: 1713. ^1H NMR ($CDCl_3$) δ: *ca.* 0.73-1.04 (3H, m), 0.90 (3H, d, J=6.5 Hz), 1.65 (3H, s), 2.30-2.74 (3H, m), 3.01 (1H, d, J=15.5 Hz), 3.65 (1H, br s), 5.69-5.83 (1H, m), 6.16 (1H, dd, J=3, 3 Hz), 7.29 (1H, dd, J=3, 2 Hz), 7.36-7.63 (3H, m), 7.63-7.87 (2H, m).

5-Hexen-2-one *N*, *N*-Dimethylhydrazone — According to the literature,[8] this was prepared in 84% yield as colorless oil, bp 86-89°C/78 mmHg. IR (neat) cm^{-1}: 1642. ^1H NMR ($CDCl_3$) δ: 1.93 (3H, s), 2.10-2.71 (4H, m), 2.40 (6H, s), 4.81-5.17 (2H, m), 5.54-6.07 (1H, m).

4-(3-Butenyl)-6,8-dimethyl-1-phenylsulfonyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (21) — An Et_2O (5 ml) solution of 5-hexen-2-one *N*, *N*-dimethylhydrazone (464 mg) was treated with 15% BuLi-hexane (1.82 ml) under Ar atmosphere at -54 – -42°C for 1.5 h. The mixture was cooled to -75°C, and to this was added dropwise a toluene (5 ml) solution of **7b** (150 mg). The whole was stirred at -75 – -66°C for 1 h and worked up as above. PTLC [hexane-EtOAc (5:2), and then hexane-CH_2Cl_2 (1:1) for the recovery] afforded crude **20** (166 mg) and **7b** (44 mg, 29%, cis/trans = 11). The crude product (**20**) (166 mg) was refluxed in 6% H_2SO_4 – 2-propanol (6 ml) for 5.5 h. The same work-up as above and PTLC [hexane-EtOAc (9:1)] gave **21** (84 mg, 45% from **7b**) and **22** (15 mg, 8% from **7b**). **21**: Colorless syrup (cis:trans=*ca.* 5:6). MS *m/z*: 379 (M^+). IR ($CHCl_3$) cm^{-1}: 1640. ^1H NMR ($CDCl_3$) δ: 1.05 and 1.30 (3H, 6:5, d each, J=7 Hz), 1.23 and 1.32 (3H, 6:5, d each, J=7 Hz), 3.00-3.48 (1H, m), 3.79-4.28, (1H, m), 4.79-5.17 (2H, m), 5.52-6.11 (1H, m), 6.66 and 6.71 (1H, 5:6, d each, J=4 Hz), 6.91 (1H, s). **22**: Colorless syrup. MS *m/z*: 397 (M^+). IR ($CHCl_3$) cm^{-1}: 1711, 1640. ^1H NMR ($CDCl_3$) δ: 0.89 (3H, d, J=7 Hz), 1.63 (3H, s), 2.59 (1H, d, J=15.5 Hz), 3.00 (1H, d, J=15.5 Hz), 3.64 (1H, br s), 4.91 (1H, br d, J=11 Hz), 4.95 (1H, br d, J=17 Hz), 5.47-5.98 (1H, m), 5.75 (1H, dd, J=3.5, 2 Hz), 6.16 (1H, dd, J=3.5, 3.5 Hz), 7.30 (1H, dd, J=3.5, 2 Hz), 7.37-7.63 (3H, m), 7.63-7.86 (2H, m).

4-(1-Butenyl)-6,8-dimethyl-1-phenylsulfonyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (24) — An EtOH (0.5 ml) solution of **21** (38 mg) and $RhCl_3 \cdot 3H_2O$ (1 mg) was gently refluxed with stirring under Ar

atmosphere for 5 h. After cooling, the mixture was evaporated to dryness and PTLC [hexane-benzene (3:2)] afforded crude **24** (36 mg, *ca.* 95%), colorless syrup. MS *m/z*: 379 (M^+). ^1H NMR ($CDCl_3$) δ: 3.01-3.56 (1H, m), 3.82-4.29 (1H, m), 6.07-6.96 (2H, m), 6.80 and 6.85 (1H, d each, J=4 Hz), 7.20 (1H, s).

(±)-Iso-trans-trikentrin B (5) and (±)-Iso-cis-trikentrin B (25) — A solution of the crude product (**24**) (36 mg) in 10% KOH – DME-MeOH-H_2O (1:1:1) (3 ml) was refluxed for 4 h. The same work-up described above and PTLC [Merck SiO_2 60 F_{254} (20 × 20 cm) plate, three sheets, hexane-DME (34:1), five times development] gave (±)-**5** (10 mg, 42% from **21**) as a more polar substance and (±)-**25** (8.5 mg, 35.5% from **21**) as a less polar substance. (±)-Iso-trans-trikentrin B (**5**): Unstable colorless oil, which turned blue on standing. HRMS Calcd for $C_{17}H_{21}N$: 239.167. Found: 239.167. IR ($CHCl_3$) cm^{-1}: 3500, 1620. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.14 (3H, t, J=7.5 Hz), 1.31 (3H, d, J=7 Hz), 1.32 (3H, d, J=7 Hz), 1.96 (1H, ddd, J=12.5, 7.5, 7.5 Hz), 2.05 (1H, ddd, J=12.5, 7.5, 3.5 Hz), 2.31 (2H, ddq J=7, 1.5, 7.5 Hz), 3.41 (1H, ddq, J=7.5, 7.5, 7 Hz), 3.53 (1H, ddq, J=7.5, 3.5, 7 Hz), 6.39 (1H, dt, J=16, 7 Hz), 6.73 (1H, dd, J=3, 2 Hz), 6.78 (1H, dt, J=16, 1.5 Hz), 7.08 (1H, s), 7.18 (1H, dd, J=3, 2.5 Hz), 8.02 (1H, br s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.0, 20.0, 20.8, 26.5, 36.1, 37.8, 43.7, 101.8, 112.5, 123.3, 125.3, 127.4 (×2), 128.5, 129.1, 132.5, 142.6. (±)-**25**: Unstable colorless oil, which turned purple on standing. HRMS Calcd for $C_{17}H_{21}N$: 239.167. Found: 239.167. IR ($CHCl_3$) cm^{-1}: 3500, 1614. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.14 (3H, t, J=7.5 Hz), 1.32 (1H, ddd, J=12.5, 8.5, 8.5 Hz), 1.38 (3H, d, J=7 Hz), 1.49 (3H, d, J=7 Hz), 2.31 (2H, ddq, J=7, 1.5, 7.5 Hz), 2.61 (1H, ddd, J=12.5, 7.5, 7.5 Hz), 3.22 (1H, ddq, J=8.5, 7.5, 7 Hz), 3.45 (1H, ddq, J=8.5, 7.5, 7 Hz), 6.39 (1H, dt, 16, 7 Hz), 6.73 (1H, dd, J=3, 2 Hz), 6.78 (1H, dt, J=16, 1.5 Hz), 7.08 (1H, s), 7.18 (1H, dd, J=3, 2.5 Hz), 8.09 (1H, br s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.0, 20.8, 21.0, 26.5, 37.2, 38.8, 44.6, 101.6, 112.3, 123.3, 125.5, 127.3, 128.1, 129.0, 132.6, 132.8, 143.1.

5-(1-Butyl)-6,8-dimethyl-1-phenylsulfonyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (27) — To a solution of LDA, prepared from diisopropylamine (0.31 ml) and 15% BuLi-hexane (1.20 ml) in THF (3 ml) under Ar atmosphere at -20°C for 10 min, was added dropwise a THF (2 ml) solution of hexanal *N*-cyclohexylimine (344 mg) and the mixture was stirred at -20°C for 45 min, and at 0°C for 15 min. It was cooled at -77°C, a toluene (5 ml) solution of **7b** (100 mg) was added, and stirring was continued at -77 – -62°C for 1h. The reaction was quenched with sat. NH_4Cl-H_2O, sat.$NaHCO_3$-H_2O was added to this, the mixture was shaken with Et_2O, and the organic layer was worked up as usual to give a residue (428 mg). This was treated with 6% H_2SO_4 – 2-propanol (12 ml) at reflux for 0.5 h. The same work-up as above and passage through silica gel afforded a mixture (287 mg). This was treated again with 6% H_2SO_4 – 2-propanol (7.5 ml) at reflux for 1 h. The same work-up as above and PTLC [hexane-EtOAc (24:1)] gave crude **27** and crude **7b**. Both were further purified by PTLC using hexane-CH_2Cl_2 (4:1) and hexane-benzene (1:4), respectively, to afford **27** (27 mg, 22.5%) and the recovery of **7b** (52 mg, 52%) (cis:trans=*ca.* 3:1). **27**: Colorless syrup. HRMS Calcd for $C_{23}H_{27}NO_2S$: 381.176. Found: 381.175. ^1H NMR ($CDCl_3$) δ: 0.19 (3H, t, J=6.5 Hz), 1.19 and 1.32 (3H, d each, J=7 Hz), 1.24 and 1.32 (3H, d each, J=7 Hz), 3.11-3.63 (1H, m), 3.88-4.37 (1H, m), 6.49 and 6.55 (1H, d each, J=4 Hz), 6.99 and 7.11 (1H, s each), 7.34 and 7.50 (1H, d each, J=4 Hz).

5-Hexenal *N*-Cyclohexylimine (28) — A THF (7.5 ml) solution of acetaldehyde *N*-cyclohexylimine (4.00 g) was added dropwise during 5 min at -20°C to a solution of LDA, prepared from diisopropylamine (5.37 ml) and 15% BuLi-hexane (23.6 ml) in THF (25 ml) under Ar atmosphere at -20°C for 15 min. The mixture was stirred at -20°C for 15 min and at 0°C for 30 min. It was cooled to -76°C and a THF (7.5 ml) solution of 4-bromo-1-butene (3.74 ml) was added during 10 min and stirring was continued at -76 – 24°C for 17 h. The reaction mixture was poured into H_2O, it was extracted with Et_2O, and the organic layer was worked up as usual. Distillation gave **28** (2.74 g, 48%) as colorless oil, bp 104-107°C/10 mmHg. IR (neat) cm^{-1}: 1665, 1640. ^1H

NMR ($CDCl_3$) δ: 1.91-2.38 (4H, m), 2.68-3.11 (1H, m), 4.91 (1H, ddt, J=10, 2, 1 Hz), 4.95 (1H, ddt, J=17, 2, 1 Hz), 5.77 (1H, ddt, J=17, 10, 6.5 Hz), 7.63 (1H, t, J=5 Hz).

5-(3-Butenyl)-6,8-dimethyl-1-phenylsulfonyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (30) — To a solution of LDA, prepared from diisopropylamine (0.30 ml) and 15% BuLi-hexane (1.06 ml) in Et_2O (2.5 ml) under Ar atmosphere at -20°C for 10 min, an Et_2O (2 ml) solution of 5-hexenal *N*-cyclohexylimine (**28**) (298 mg) was added and the mixture was stirred at -20°C for 15 min and at 0°C for 30 min. The mixture was cooled at -79°C, a toluene (4.5 ml) solution of **7b** (150 mg) was added dropwise, and stirring was continued at -79 – -61°C for 1 h. The reaction was quenched with sat. NH_4Cl-H_2O, sat. $NaHCO_3$-H_2O was added to this, the mixture was extracted with Et_2O, and the organic layer was worked up as usual to leave a residue (441 mg). This was dissolved in DME (3 ml) and 10% oxalic acid-H_2O (6 ml) was added to this. After stirring at room temperature (18°C) for 16 h, sat. $NaHCO_3$-H_2O was added at 0°C. Extraction with CH_2Cl_2 and usual work-up gave a residue containing **29** (322 mg). It was treated with 6% H_2SO_4 – 2-propanol (9 ml) at reflux for 1 h. The same work-up as above and PTLC [hexane-EtOAc (24:1)] afforded crude **30** and crude **7b**. Both were further purified by PTLC using hexane-CH_2Cl_2 (3:1) and hexane-CH_2Cl_2 (1:1), respectively, to give **30** (65 mg, 36%, cis/trans = *ca.* 1.4) and the recovery of **7b** (38 mg, 25%, cis:trans=5:2). **30:** Colorless syrup HRMS Calcd for $C_{23}H_{25}NO_2S$: 379.161. Found: 379.160. IR ($CHCl_3$) cm^{-1}: 1638. ^1H NMR ($CDCl_3$) δ: 1.21 and 1.32 (3H, 1:1.4, d each, J=7 Hz), 1.24 and 1.32 (3H, 1:1.4, d each, J=7 Hz), 1.79-2.03 (2H of the trans isomer, m), 3.09-3.58 (1H, m), 3.90-4.32 (1H, m), 4.81-5.16 (2H, m), 5.60-6.14 (1H, m), 6.51 and 6.57 (1H, 1:1.4, d each, J=4 Hz), 7.02 and 7.13 (1H, 1:1.4, s each), 7.39 and 7.52 (1H, 1.4:1, d each, J=4 Hz).

5-(1-Butenyl)-6,8-dimethyl-1-phenylsulfonyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (31) — An EtOH (1 ml) solution of **30** (20 mg) containing $RhCl_3 \cdot 3H_2O$ (0.8 mg) was heated in a sealed tube under Ar atmosphere at 100°C for 50 h. After cooling to 0°C, sat. $NaHCO_3$-H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and PTLC [Merck SiO_2 60 F_{254} (20 × 20 cm) plate, three sheets, hexane-DME (79:1), seven times development] yielded **31** (16 mg, 80%, cis:trans=*ca.* 1.4:1) as colorless syrup. HRMS Calcd for $C_{23}H_{25}NO_2S$: 379.161. Found: 379.160. IR ($CHCl_3$) cm^{-1}: 1647. ^1H NMR ($CDCl_3$) δ: 1.04 (3H, t, J=7 Hz), 1.18 and 1.28 (3H, 1:1.4, d each, J=7 Hz), 1.25 and 1.33 (3H, 1:1.4, d each, J=7 Hz), 1.91 (2H of the trans isomer, dd, J=6.5, 6.5 Hz), 2.21 (2H, dq, J= 6, 7 Hz), 2.49 (1H of the cis isomer, ddd, J=13, 9, 9 Hz), 3.18-3.64 (1H, m), 3.91-4.32 (1H, m), 6.06 and 6.13 (1H, 1:1.4, dt each, J=16, 6 Hz), 6.51 (1H, br d, J=16 Hz), 6.54 and 6.58 (1H, 1:1.4, d each, J=4 Hz).

(±)-cis-Trikentrin B (3) and (±)-trans-Trikentrin B (4) — The compound (**31**) (16 mg) was treated with 10% KOH – DME-MeOH-H_2O (1:1:1) (2.4 ml) at gentle reflux for 3 h. The mixture was worked up as above and purification by PTLC [Merck SiO_2 60 F254 (20 × 20 cm) plate, two sheets, hexane-DME (69:1), six times development] afforded (±)-**3** (5 mg, 50%) as a more polar substance and (±)-**4** (3.5 mg, 35%) as a less polar substance. (±)-cis-Trikentrin B (**3**): Unstable colorless syrup, which turned blue on prolonged storage. HRMS Calcd for $C_{17}H_{20}N$: 239.167. Found: 239.168. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.11 (3H, t, J=7.5 Hz), 1.34 (3H, d, J=7 Hz), 1.44 (3H, d, J=7 Hz), 1.54 (1H, ddd, J=13, 2.5, 2.5 Hz), 2.25 (2H, ddq, J=7, 1.5, 7.5 Hz), 2.70 (1H, ddd, J=13, 9, 9 Hz), 3.47 (1H, ddq, J=9, 2.5, 7 Hz), 3.49 (1H, ddq, J=9, 2.5, 7 Hz), 6.17 (1H, dt, J=16, 7 Hz), 6.52 (1H, dd, J=3, 2 Hz), 6.59 (1H, dt, J=16, 1.5 Hz), 7.13 (1H, dd, J=3, 2.5 Hz), 7.61 (1H, s), 7.93 (1H, br s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.0, 22.5, 24.2, 26.3, 37.0, 38.4, 41.7, 103.1, 115.6, 123.7, 127.4 (×2), 127.7, 129.0, 131.0, 131.9, 140.6. (±)-trans-Trikentrin B (**4**): Unstable colorless syrup, which turned blue on prolonged storage. HRMS Calcd for $C_{17}H_{20}N$: 239.167. Found: 239.166. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.11. (3H, t, J=7 Hz), 1.18 (3H, d, J=7 Hz), 1.46 (3H, d, J=7 Hz), 1.95 (1H, ddd, J=12.5, 9.5, 8 Hz), 2.08 (1H, ddd, J=12.5, 7.5, 1.5 Hz), 2.25 (2H, ddq, J=6.5, 1.5, 7 Hz), 3.52 (1H, ddq, 8, 1.5, 7 Hz), 3.66 (1H, ddq, J=9.5, 7.5, 7 Hz), 6.18 (1H, dt, J=16, 6.5 Hz), 6.52 (1H, dd,

J=3, 2 Hz), 6.59 (1H, dt, J=16, 1.5 Hz), 7.13 (1H, dd, J=3, 2.5 Hz), 7.61 (1H, s), 8.00 (1H, br s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.1, 20.1, 21.1, 26.4, 36.3, 37.5, 43.6, 103.0, 115.2, 123.7, 127.0, 127.1, 128.0, 128.1, 131.1, 132.1, 141.5.

Dimethylcyclopentanones (37, 38, 39, and 40) — A MeOH (60 ml) solution of the mixture (**35** and **36**) (8.79 g), prepared from (*R*)-(+)-pulegone (**32**) according to the literature,[21] was treated with NaOMe (3.35 g) under Ar atmosphere at -20°C for 1 h. To this was added MeI (17.6 ml) dropwise and the mixture was stirred at -20 – 20°C for 14.5 h. It was poured into sat. NH_4Cl-H_2O, the whole was extracted with CH_2Cl_2, and the organic layer was worked up as usual. Distillation afforded a mixture of the methylated derivatives (8.84 g, 92%), colorless oil, bp 86-88°C/6 mmHg. IR (neat) cm^{-1}: 1753, 1730. This mixture (8.24 g) was heated in 47% HBr-H_2O (16 ml) at 120°C for 6 h. After cooling, it was poured into ice-water and the mixture was extracted with Et_2O. Washing of the organic layer with sat. $NaHCO_3$-H_2O, ususal work-up, and distillation afforded a mixture of **37**, **38**, **39**, and **40** (4.16 g, 77%), colorless oil, bp 74-76°C/58 mmHg. IR (neat) cm^{-1}: 1738. ^1H NMR ($CDCl_3$, 400 MHz) of **37** δ: 1.09 (3H, d, J=7 Hz), 1.13 (3H, d, J=6.5 Hz); **38** δ: 1.08 (3H, d, J=7 Hz), 1.10 (3H, d, J=7 Hz); **39** δ: 1.06 (3H, d, J=6.5 Hz), 1.16 (3H, d, J=6 Hz); **40** δ: 0.91 (3H, d, J=7 Hz), 0.98 (3H, d, J=7 Hz).

Trimethylsilyl Enol Ethers (41 and 42) — According to the procedure used for preparing **10**, the above mixture of **37**, **38**, **39**, and **40** (3.94 g) was converted into a mixture of **41** and **42** (5.82 g, 90%) as colorless oil, bp 78-90°C/48 mmHg. IR (neat) cm^{-1}: 1640. ^1H NMR ($CDCl_3$) δ: 0.19 (9H, s), 4.49 (1H, br s).

(2*R*, 3*R*)-3,5-Dimethyl-2-(1-phenylsulfonyl-2-pyrrolyl)cyclopentanones (44 and 45) and 43 — Employing the procedure used for preparing **7b**, a CH_2Cl_2 (10 ml) solution of the mixture of **41** and **42** (2.660 g) and an EtOAc (80 ml) solution of $SnCl_2$ (2.746 g) was added dropwise to a photooxygenated solution of **6** (2.498 g) and methylene blue (60 mg) in CH_2Cl_2 (180 ml) at -40°C. After being stirred at -40 – -47°C for 1 h, the reaction mixture was warmed gradually up to 0°C during 1.5 h. The same work-up as before and purification by the repeated column chromatography [hexane-CH_2Cl_2 (3:2)] afforded a mixture of **44** and **45** (1.426 g, 37%) as more polar substances and **43** (726 mg, 19%) as less polar substances along with the recovery of **6** (43 mg, 2%). **44** + **45**: Colorless syrup, (cis:trans=*ca.* 4:1). HRMS Calcd for $C_{17}H_{19}NO_3S$: 317.109. Found: 317.106. For the spectral data, refer to those of **7b**. **43**: Colorless syrup. HRMS Calcd for $C_{17}H_{19}NO_3S$: 317.109. Found: 317.108. IR ($CHCl_3$) cm^{-1}: 1741. ^1H NMR ($CDCl_3$, 400 MHz) of two major isomers δ: 1.11 and 1.12 (3H, d each, J=6 Hz), 1.13 and 1.16 (3H, d each, J=6 Hz), 3.91 and 4.11 (1H, dd each, J=12, 8 Hz, and J=9.5, 3.5 Hz), 5.77 and 5.98 (1H, dd each, J=3.5, 1.5 Hz), 6.20 and 6.25 (1H, dd each, J=3.5, 3.5 Hz), 7.21 and 7.25 (1H, dd each, J=3.5, 1.5 Hz).

(6*S*, 8*R*)- and (6*R*, 8*R*)-6,8-Dimethyl-4-ethyl-1-phenylsulfonyl-1,6,7,8-tetrahydrocyclopent-[*g*]indoles (48) — Using the procedure used for preparing **16a** and **16b**, a toluene (5 ml) solution of the mixture of **44** and **45** (191 mg) was treated with a solution of lithium salt of 2-butanone *N*, *N*-dimethylhydrazone, prepared from the hydrazone (483 mg) and 15% BuLi-hexane (2.40 ml) in Et_2O (5 ml). The same work-up as before and PTLC [hexane-EtOAc (3:1)] gave **46** (158 mg, 61%) as colorless syrup and the recovery of **44** and **45** (*ca.* 11:1) (62 mg, 32%). The mixture (**46**) (158 mg) was treated with 6.5% H_2SO_4 – 2-propanol (9 ml) at reflux for 14 h. The same work-up as before and PTLC [hexane-EtOAc (9:1)] afforded **48** (94 mg, 73%, cis:trans=*ca.* 4:3) as colorless syrup and **47** (16 mg, 12%), colorless syrup, $[\alpha]_D^{24}$ –29.9° (*c* 0.88, $CHCl_3$).

(–)-cis-Trikentrin A (49) and (–)-trans-Trikentrin A (50) — The above mixture (**48**) (94 mg) was hydrolyzed with 10% KOH – DME-MeOH-H_2O (1:1:1) (6 ml) at 85-90°C for 6.5 h. The same work-up as before and purification by column chromatography [hexane-CH_2Cl_2 (19:1)] afforded **49** (29.5 mg, 52%) and **50** (21 mg, 37%). (–)-cis-Trikentrin A (**49**): Unstable colorless syrup. HRMS Calcd for $C_{15}H_{19}N$: 213.152.

Found: 213.150. $[\alpha]_D^{24}$ –68.6° (*c* 1.03, $CHCl_3$) [lit.[1] $[\alpha]_D$ +48° (*c* 2.47, $CHCl_3$)]. (–)-trans-Trikentrin A (**50**): Unstable colorless syrup. HRMS Calcd for $C_{15}H_{19}N$: 213.152. Found: 213.150. $[\alpha]_D^{24}$ –26.8° (*c* 0.68, $CHCl_3$) [lit.[1] $[\alpha]_D$ +23.3° (*c* 1.0, $CHCl_3$)].

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