Preparation of Alkyl-Substituted Indoles in the Benzene Portion. Part 10.[1] Synthesis of 4- and/or 5-Alkylated 1,6,7,8-Tetrahydrocyclopent[*g*]indoles, Model Compounds for Herbindole and Trikentrin Syntheses

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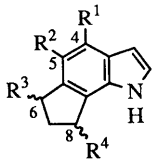
Synthetic pathways leading to model compounds 25, 27, 33, 20d, 32b, 37, and 42 for the marine alkaloids, herbindoles and trikentrins (1b—i), are presented. *p*-Toluenesulfonic acid-mediated indole cyclization reactions, 19→20 and 38→39, assisted with thiols such as benzylthiol or thiophenol, are key steps for preparation of the compounds having the 1,6,7,8-tetrahydrocyclopent[*g*]indole structure. Novel reactions of the phenylsulfone group in 20c and 20e with allyltrimethylsilane in the presence of dichloroethylaluminum as well as with trimethylaluminum, are explained in terms of participation of an intermediary reactive species 29.

Keywords polyalkylindole synthesis; sulfone substitution; herbindole trikentrin model; acid-induced indole cyclization reaction; organoaluminum derivative

1,6,7,8-Tetrahydrocyclopent[*g*]indole (**1a**) is a fundamental structural unit of marine products, trikentrins[2] and herbindoles,[3] isolated from the sponges *Trikentrion flabelliforme* and *Axinella* sp., respectively. Variously alkyl- and alkenyl-substituted derivatives of **1a** at the 4-, 5-, 6-, and 8-positions shown in Chart 1 constitute the chemical structures of *cis*-trikentrin A (**1b**), *trans*-trikentrin A (**1c**), *cis*-trikentrin B (**1d**), *trans*-trikentrin B (**1e**), iso-*trans*-trikentrin B (**1f**), herbindole A (**1g**), herbindole B (**1h**), and herbindole C (**1i**). All five trikentrins have been synthesized by us in the racemic form, and the absolute structures of *cis*- and *trans*-trikentrins A (**1b** and **1c**) were established by a chiral synthesis of their enantiomers.[4,5]

In those studies, we employed an acid-catalyzed indole cyclization reaction of 2-substituted pyrrole derivatives **2** to furnish **3** (R^1 = alkyl, R^2 = H; or R^1 = H, R^2 = alkyl) as a key step for realization of our efficient synthesis of trikentrins (Chart 2). We next applied this reaction step to the synthesis of herbindoles. Aiming at the synthesis of herbindole B (**1h**), dimethylhydrazone **5a** was prepared from pyrrolylcyclopentanone **4** by condensation with the lithium salt of 3-pentanone *N*,*N*-dimethylhydrazone, and submitted to the above indole cyclization reaction. However, the indole formation did not take place, and only the ketone **5b** and enone **6** were obtained. The reason for this unsuccessful result with addition of one methyl group to the precursor **2** (that is $R^1 = R^2$ = alkyl) is ascribed to an increased steric hindrance around the reaction site. The cyclopentane ring in **5a** carries many substituents and two spatially congested functions, a 1-(phenylsulfonyl)-2-pyrrolyl group and a heavily substituted alkyl side chain, are located close together. Another methyl group may destroy both geometrical and conformational freedoms for the indole cyclization in the reaction intermediates, and consequently **5b** and **6** remain uncyclized. Therefore we had to look for an alternate route to herbindoles.

In the previous paper of this series, we reported an effective preparative method for 4-alkylindoles.[6] This method is based on a similar acid-catalyzed cyclization of 3-substituted pyrroles **8** to afford indoles **9**, and variously functionalized, important 4-substituted indoles are readily accessible from the common precursors **7** in a few steps (Chart 3). When we adopt this procedure for herbindole synthesis, necessary substrates for the indole cyclization can be depicted as **10** (R^1 = Me), where the absolute



	R^1	R^2	R^3	R^4
1a	H	H	H	H
1b[a,c]	Et	H	β-Me	β-Me
1c[a]	Et	H	α-Me	β-Me
1d[b]	H	(*E*)-1-butenyl	β-Me	β-Me
1e[b]	H	(*E*)-1-butenyl	α-Me	β-Me
1f[b]	(*E*)-1-butenyl	H	α-Me	β-Me
1g[b]	Me	Me	α-Me	α-Me
1h[b]	Et	Me	α-Me	α-Me
1i[b]	(*E*)-1-butenyl	Me	α-Me	α-Me

a) Absolute structures were determined previously. See reference 4.
b) Absolute structures were determined or estimated in the present study. See the following paper.
c) Absolute structure was confirmed in the present study. See the following paper.

Chart 1

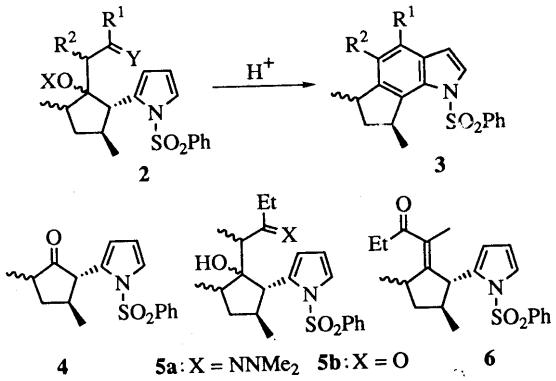


Chart 2

configuration of the dimethyl groups is assumed to be as shown by analogy with that of *cis*-trikentrin A. In the precursor molecules **10** (R^1 = Me), the cyclopentane ring is separated from the pyrrole part by a two carbon unit, so that the steric environment is expected to be much more suitable for the cyclization reaction. We first selected simplified compounds **10** (R^1 = H) for the present model study to see whether the cyclization reaction **10**→**11** (R^1 = H) really takes place.

A. Model Study for the Synthesis of Herbindole A, Herbindole B, and Herbindole C Compounds **10** (R^1 = H), *i.e.*, **19a** and **19b**, were synthesized as follows (Chart 4). According to the literature,[7,8] 1-cyclopentenylmethanol **12** was prepared from commercially available 1,2-dihydroxycyclohexane (a mixture of *cis* and *trans* isomers) by successive treatment with sodium metaperiodate, potassium hydroxide, and sodium borohydride, and **12** was submitted to the Claisen rearrangement using triethyl orthopropionate[9] in the presence of pivalic acid. The cyclopentylpropionate **13a**, obtained in 82% yield, was treated with lithium diisopropylamide (LDA) and coupled with 3-formyl-1-(phenylsulfonyl)pyrrole[6b] (**14**) to furnish **15a** in 96% yield. This was oxidized with manganese dioxide to the β-ketoester **16a** in 84% yield and its deethoxycarbonylation was effected only by heating with lithium chloride in aqueous hexamethylphosphoramide (HMPA)[10] to give **17a** in 70% yield. With a model synthesis of herbindole C (**1i**) in mind, an *n*-butyl group was introduced into the ketone group of **17a** by treatment with *n*-butyllithium. The yield of the product **18a** was unexpectedly low at 50%, presumably due to the fact that *n*-butyllithium behaved at the same time as a strong base to abstract hydrogens adjacent to the ketone group and/or from the 1-(phenylsulfonyl)pyrrole group. On the other hand, reaction of **17a** with a soft base such as (phenylsulfonyl)methyllithium proceeded satisfactorily to give **18b** in 90% yield. Both **18a** and **18b** were oxidized with sodium metaperiodate in the presence of a catalytic amount of osmium tetroxide, and the desired substrates **19a** and **19b** for the indole cyclization were produced in 71% and 72% yields, respectively.

The indole cyclization was attempted by heating **19a** in 6% sulfuric acid-containing 2-propanol (Chart 5).[4,11] The reaction was complete within a short period but the formation of a hitherto unencountered by-product **20b** was observed in 21% yield in addition to the expected indole **20a** in 67% yield. Application of this cyclization condition to the phenylsulfone **19b** gave a worse result, and the expected indole **20c** was obtained in only 11% yield. Major products were estimated from the ^{1}H-NMR analysis to be mixtures of dehydration compounds of a *Z* isomer **21** and α,β-unsaturated sulfones **22**, which remained uncyclized under the sulfuric acid conditions. So the catalyst was changed to *p*-toluenesulfonic acid, and **19b** was heated in benzene using a Dean–Stark apparatus.[12] The same mixture of dehydration compounds **21** and **22** was still produced, but the yield of **20c** was enhanced to 73%. In order to assist the double bond isomerization in uncyclizable compounds, benzylthiol was added to the above reaction mixture. This stemmed from the idea that an acid-catalyzed addition of benzylthiol to the double bond of **23**, followed by successive elimination would make a favorable isomer **24** for the indole cyclization rich in the reaction mixture. By this procedure, the indoles **20a** and **20c** were produced from **19a** and **19b** in excellent yields of 94% and 93%, respectively. Alkaline hydrolysis of **20a** afforded one of the model compounds, **25**, in 93% yield.

When analogous alkaline hydrolysis of **20c** was carried out with sodium hydroxide in a (2:1:1) mixture of dimethoxyethane (DME), methanol and water, the desulfonation did occur readily to afford the expected product **26a** in 33% yield (Chart 6). In addition to this,

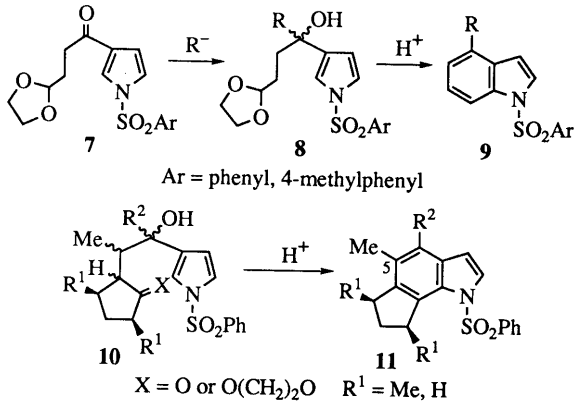


Chart 3

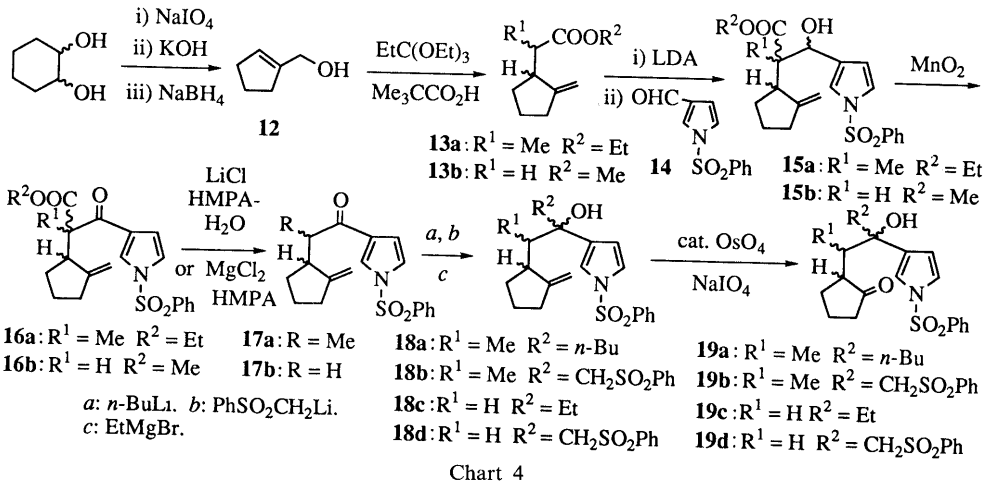


Chart 4

however, concomitant methanolysis of the phenylsulfone group at the side chain took place, and a methoxy derivative **26b** was obtained in 54% yield as the major reaction product. So removal of the protecting group was tried by application of our magnesium–methanol procedure.[13] Conveniently, the phenylsulfonyl group not only at the indole nitrogen but also at the alkyl side chain was reductively split off quite readily and the required model compound **27** for herbindole A (**1g**) was directly obtained in 92% yield.

These phenomena that the side chain phenylsulfone group in **20c** substitutes readily with nucleophiles to afford

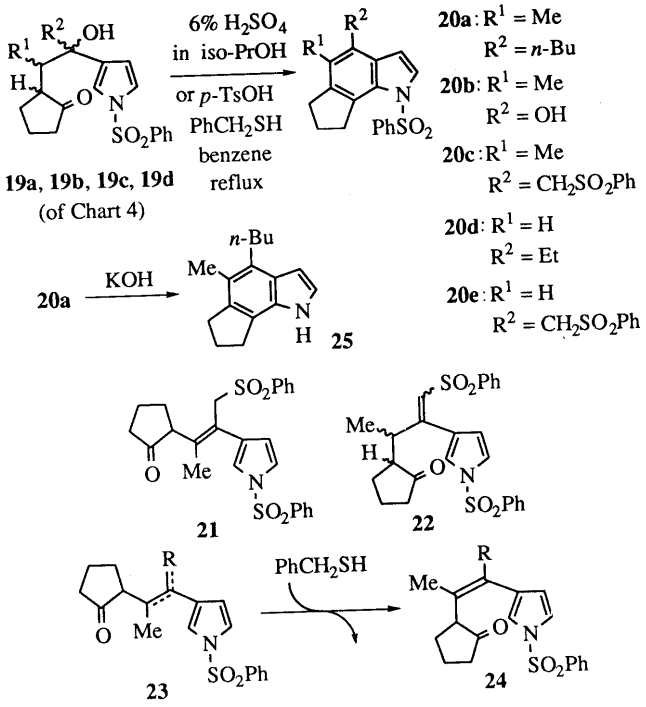


Chart 5

26b and **27** might be explained in terms of its special location exerting pseudo-gramine character, shown by participation of the process **28**→**29**. In principle, this character of the sulfone group resembles the behavior involved in Lewis acid-catalyzed nucleophilic substitutions of allylsulfones,[14] α-sulfonyl sulfides,[15,16] α-sulfonyl selenides,[16] and α-sulfonyl acylamines.[17] Therefore replacement of the sulfone group of **20c** with the allyl substituent was next studied using allyltrimethylsilane as a nucleophile in the presence of a variety of Lewis acids under the reaction conditions shown in Table I. Dichloroethylaluminum afforded the best result, giving **30a** in 90% yield.

Generality of this reaction was tested by applying it to a simpler substrate. 1-(Phenylsulfonyl)-4-[(phenylsulfonyl)methyl]indole (**34**),[6b] prepared from **7** (Ar = phenyl) by way of **8** (R = $PhSO_2CH_2$, Ar = phenyl), was treated with allyltrimethylsilane in the presence of dichloroethylaluminum in dichloromethane at −20 °C. Although the reaction required a longer time of stirring (3 h) for completion, the expected indole **35** was obtained in 79% yield. This kind of special affinity of the sulfone group for an aluminum species[18] suggested the use of trimethylaluminum for direct replacement of the side chain sulfone group by the methyl group.[19] In fact, the above compound

Table I. Lewis Acid-Catalyzed Reaction of Allyltrimethylsilane (6—12 molar eq) with 4-Indolylmethyl Phenyl Sulfone **20c** in Dichloromethane

Lewis acid (molar eq)	Temperature (°C)	Time	**30a** (yield %)	Recovery of **20c** (%)
$BF_3 \cdot OEt_2$ (4)	0—20	2.5 h	0	92
$Zn(OTf)_2$ (6)	Reflux	1.5 h	0	93
$SnCl_4$ (3)	−20—18	1.75 h	Trace	83
$TiCl_4$ (4)	−20	20 min	48	0
$AlCl_3$ (5)	−20—18	1.5 h	66	0
$EtAlCl_2$ (4)	−20	30 min	90	0

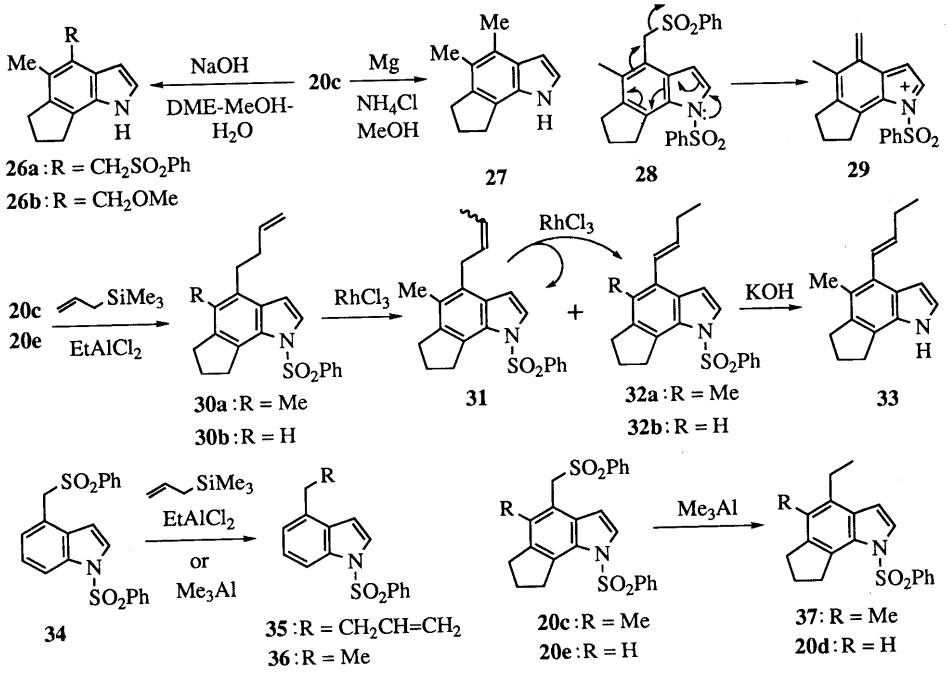


Chart 6

34 was changed to **36** in 71% yield, when refluxed in dichloromethane with this reagent for 20 h, accompanied with the recovery of **34** in 20% yield. Therefore this method was applied to **20c**, and the model compound **37**, aiming at herbindole B (**1h**), was prepared in 84% yield by stirring **20c** with trimethylaluminum at room temperature for 1 h.

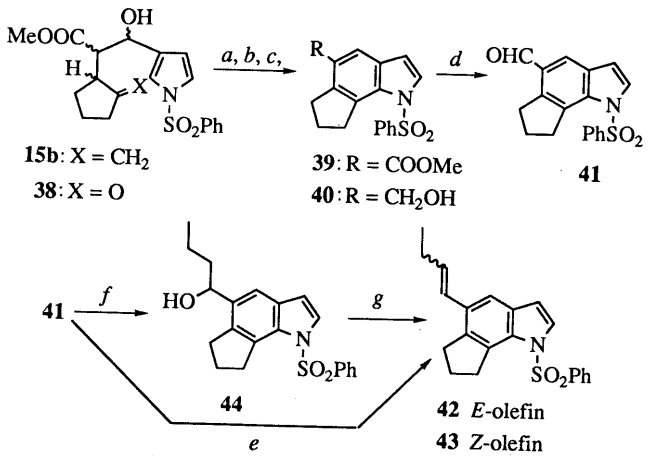
For the synthesis of the model compound **33**, corresponding to herbindole C (**1i**), migration of the terminal double bond of **30a** is necessary. This was effected as in the previous trikentrin B synthesis[4b] by heating an ethanol solution of **30a** with rhodium(III) chloride in a sealed tube at 100 °C for 50 h. Even with this forcing condition, intermediary compounds **31** as a mixture of two geometric isomers were isolated in 22% yield, together with the requisite *E* isomer **32a** in 67% yield. The mixture **31** was further heated with rhodium(III) chloride under the same conditions to provide an additional crop of **32a** in 62.5% yield along with the recovery of **31** in 25% yield. Alkaline hydrolysis of **32a** gave **33** in 91% yield.

B. Model Study for the Synthesis of Trikentrins A and Trikentrins B The successful model study for herbindoles made it possible to consider a chiral synthesis of trikentrins according to a new approach. For instance, in the indole structure **11** (R^1 = Me) (Chart 3), a compound lacking the methyl group at the 5 position represents the nitrogen-protected form of *cis*-trikentrin A (**1b**), when R^2 is the ethyl group. So if we start a similar kind of synthesis from a Claisen rearrangement product **13b**, this would represent a model study for the chiral synthesis of trikentrins.

Compound **13b**[20] was condensed with **14** as above to obtain **15b** in 96% yield (Chart 4). Oxidation of **15b** with manganese dioxide proceeded without difficulty to afford the β-keto-ester **16b** in 89% yield. Removal of the methoxycarbonyl group in this case required different reaction conditions compared to the above **16a**, and this step was best carried out by heating **16b** in HMPA with magnesium chloride[21] to produce **17b** in 78% yield. Reactions of **17b** with ethylmagnesium bromide and lithiomethyl phenyl sulfone proceeded readily, and **18c** and **18d** were obtained in 89% and 98% yields. These were oxidized to the precursor molecules **19c** and **19d** for the indole cyclization in 76% and 71% yields, respectively. Refluxing benzene solutions of **19c** and **19d** with a catalytic amount of *p*-toluenesulfonic acid in the presence of benzylthiol smoothly afforded the indole derivatives **20d** and **20e** in respective yields of 92% and 90% (Chart 5). The former compound **20d** corresponds to a model for *cis*-trikentrin A (**1b**).

The latter sulfone **20e** was converted into another model **32b** for iso-*trans*-trikentrin B (**1f**) by reaction with allyltrimethylsilane in the presence of dichloroethylaluminum to give **30b** in 86% yield, followed by treatment of **30b** with rhodium(III) chloride in refluxing ethanol for 8 h to afford directly **32b** in 82% yeild (Chart 6). An alternative route for the formation of the *cis*-trikentrin A model **20d** was opened by the reaction of **20e** with trimethylaluminum, and **20d** was obtained from **20e** in 88% yield.

The above transformation passed through the hydroxy-ester **15b**. When we utilize the ester group of **15b** as a handle to form the *E*-butenyl side chain, a model compound **42** for *cis*- and *trans*-trikentrins B (**1d** and **1e**) can be synthesized as shown in Chart 7. The indole-5-carboxylate **39** was synthesized from **15b** by converting the *exo*-methylene group into a ketone group, as in **38**, in 78% yield, followed by the indole cyclization reaction using thiophenol this time in 80% yield. The ester **39** was changed to the aldehyde **41** by way of the alcohol **40** using reduction with lithium aluminum hydride at low temperature (to avoid reductive cleavage of the sulfonamide) in 94% yield and subsequent oxidation with manganese dioxide in 94% yield. At first, elongation of the alkyl side chain was carried out with the Wittig reagent. However, the compound **43** having *Z* configuration was produced as a major product in 42% yield, together with an *E* derivative **42** in 32% yield, and attempted isomerization of the double bond from **43** to **42** was unsuccessful. Therefore, **41** was reacted with *n*-propylmagnesium bromide and the product **44** obtained in 91% yield, accompanied with the formation of **40** in 8.5% yield, was dehydrated by heating with a catalytic amount of *p*-toluenesulfonic acid in benzene to afford the desired *E*-butenyl derivative **42** in 92% yield as the sole reaction product.



a: cat. OsO_4, $NaIO_4$. *b*: cat. *p*-TsOH, PhSH, benzene, reflux. *c*: $LiAlH_4$. *d*: MnO_2. *e*: i) Ph_3P=CHEt, ii) NaH. *f*: *n*-PrMgBr. *g*: *p*-TsOH, benzene, reflux.

Chart 7

In summary two findings are noteworthy. i) A preparative method of 1,6,7,8-tetrahydrocyclopent[*g*]-indole was developed using *p*-toluenesulfonic acid-mediated indole cyclization reactions **19**→**20** and **38**→**39** as key steps. Addition of benzylthiol or thiophenol to the reaction mixture was essential for completion of the cyclization, because unfavorable double bond isomers such as **21** and **22** remained uncyclized without the thiol. ii) The phenylsulfone group at the side chain of **20c** and **20e** was substituted with an allyl or methyl group by treatment with allyltrimethylsilane in the presence of dichloroethylaluminum or trimethylaluminum. This unprecedented phenomenon involving the sulfone function at the 4-indolylmethyl group can be explained in terms of the special location of the sulfone, which exerts a pseudo-gramine character (**28**→**29**). Employing these reactions, variously substituted 1,6,7,8-tetrahydrocyclopent[*g*]indole derivatives, **25**, **27**, **33**, **20d**, **32b**, **37**, and **42**, were

synthesized as models of the natural products, herbindoles and trikentrins **1b**—**i**. Enantio-defined syntheses aiming at establishment of the absolute structures of the natural products are described in the following paper.[22]

Experimental

Melting points were determined on Yanagimoto micro-melting point apparatus without correction. MS and high-resolution MS (HRMS) were recorded on a Hitachi M-80B spectrometer at an ionizing voltage of 70 eV, and figures in parentheses indicate the relative intensities. GC-MS spectra were measured using an attached column Hitachi OV-1. IR spectra were measured on a Hitachi 215 spectrophotometer. ^{1}H-NMR spectra were obtained on a Varian EM 390 (90 MHz) spectrometer, unless otherwise specified, in $CDCl_3$ with tetramethylsilane as an internal reference. Column chromatography was conducted on silica gel, Fuji Davison BW 200, and preparative TLC (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 of the organic layers with water or brine, drying over anhydrous Na_2SO_4, and evaporating off the solvents under reduced pressure.

Ethyl α-Methyl-2-methylene-1-cyclopentaneacetate (13a) A solution of **12** (6.99 g, 71.3 mmol) and pivalic acid (0.436 g, 4.27 mmol) in $EtC(OEt)_3$ (37.7 g, 214 mmol) was heated at 130 °C for 3 h, while EtOH generated during the reaction was removed by distillation. Saturated $NaHCO_3$–H_2O was added at 0 °C, then the whole was extracted with Et_2O, and worked up as usual. From the residue, $EtC(OEt)_3$ (23.7 g) was recovered by distillation, and the remainder was purified by column chromatography [hexane–EtOAc (19 : 1)] to afford **13a** (10.7 g, 82%) as a colorless oil. GC-HRMS Calcd for $C_{11}H_{18}O_2$: 182.1306. Found: 182.1304. GC-MS *m/z*: 182 (M^+, 8), 109 (100), 81 (64). IR (neat) cm^{-1}: 1735, 1650. ^{1}H-NMR δ: 1.07 (3H, d, *J* = 7 Hz), 1.24 (3H, t, *J* = 7 Hz), *ca.* 1.24—2.13 (4H, m), 2.13—2.47 (2H, m), 2.58 (1H, dq, *J* = 7, 7 Hz), *ca.* 2.58—2.96 (1H, m), 4.11 (2H, q, *J* = 7 Hz), 4.66—4.83 (1H, m), 4.83—4.99 (1H, m).

Ethyl (αξ,βξ)-β-Hydroxy-α-methyl-α-[(ξ)-2-methylenecyclopentyl]-1-(phenylsulfonyl)-1*H*-pyrrole-3-propanoate (15a) An LDA solution was prepared from iso-Pr_2NH (3.20 ml, 22.9 mmol) and 15% *n*-BuLi (12.30 ml, 19.2 mmol) in tetrahydrofuran (THF) (40 ml) at −20 °C for 20 min under an Ar atmosphere. This was cooled to −82 °C and a solution of **13a** (3.495 g, 19.2 mmol) in THF (5 ml) was added dropwise. The mixture was stirred at −82—−69 °C for 45 min, and then a solution of **14** (2.050 g, 8.72 mmol) in THF (5 ml) was added dropwise. The whole was further stirred at −69—−59 °C for 1 h. Saturated NH_4Cl–H_2O was added, then the mixture was extracted with Et_2O, and worked up as usual. Purification by column chromatography [hexane–EtOAc (5 : 1)] afforded **15a** (3.488 g, 96% calculated from **14**) as a colorless syrup. HRMS Calcd for $C_{22}H_{27}NO_5S$: 417.1608. Found: 417.1632. MS *m/z*: 417 (M^+, 1), 276 (13), 235 (79), 182 (32), 141 (90), 109 (55), 77 (100), 51 (87). IR ($CHCl_3$) cm^{-1}: 1717, 1643. ^{1}H-NMR of major and minor diastereomers (*ca.* 2 : 1) δ: 1.07 and 1.10 (3H, t each, *J* = 7 Hz), 1.10 and 0.89 (3H, s each), *ca.* 1.10—2.52 (7H including one OH, m), 2.80—3.12 and 3.12—3.46 (1H, m each), 3.89 and 4.01 (2H, q each, *J* = 7 Hz), 4.29—5.14 (3H, m), 6.17—6.30 and 6.07—6.17 (1H, m each), 6.91—7.12 (2H, m), 7.32—7.70 (3H, m), 7.70—7.91 (2H, m).

Methyl (αξ,βξ)-β-Hydroxy-α-[(ξ)-2-methylenecyclopentyl]-1-(phenylsulfonyl)-1*H*-pyrrole-3-propanoate (15b) Similarly, the lithium enolate of **13b** (320 mg, 2.08 mmol) was condensed with **14** (201 mg, 0.855 mmol) to provide **15b** (319 mg, 96% calculated from **14**) as a colorless syrup. MS *m/z*: 235 (9), 141 (16), 77 (100), 51 (48), 39 (62). IR ($CHCl_3$) cm^{-1}: 1728, 1646. ^{1}H-NMR δ: 1.07—2.04 (4H, m), 2.04—2.44 (2H, m), 2.62—3.26 (3H including OH, m), 3.26 and 3.36 (3H, s each), 4.62—5.08 (3H, m), 6.17—6.36 (1H, m), 7.02—7.18 (2H, m), 7.29—7.67 (3H, m), 7.67—7.92 (2H, m).

Ethyl (αξ)-α-Methyl-α-[(ξ)-2-methylenecyclopentyl]-β-oxo-1-(phenylsulfonyl)-1*H*-pyrrole-3-propanoate (16a) A suspension of **15a** (148 mg, 0.355 mmol) and MnO_2 (926 mg, 10.6 mmol) in CH_2Cl_2 (12 ml) was refluxed for 2 h. Inorganic materials were filtered off through a Celite bed and washed with CH_2Cl_2. The combined organic layer was concentrated *in vacuo*, and the residue was purified by PTLC [hexane–EtOAc (5 : 1)] to afford **16a** (123 mg, 84%) as a colorless syrup, which later crystallized in part. Repeated recrystallization from Et_2O–hexane gave colorless prisms, mp 95—96 °C of a major isomer. *Anal.* Calcd for $C_{22}H_{25}NO_5S$: C, 63.59; H, 6.07; N, 3.37. Found: C, 63.52; H, 6.08; N, 3.45. HRMS Calcd for $C_{22}H_{25}NO_5S$: 415.1452. Found: 415.1450. MS *m/z*: 415 (M^+, 4), 342 (6), 274 (29), 234 (100), 141 (36), 77 (94). IR ($CHCl_3$) cm^{-1}: 1729, 1672. ^{1}H-NMR δ: 0.97 (3H, t, *J* = 7 Hz), 1.12—2.55 (6H, m), 1.36 (3H, s), 3.35—3.74 (1H, m), 4.00 (2H, q, *J* = 7 Hz), 4.66, 4.89 and 5.01 (2H, br s each), 6.67 (1H, dd, *J* = 3.5, 1.5 Hz), 7.06 (1H, dd, *J* = 3.5, 2.5 Hz), 7.36—7.76 (3H, m), 7.76—7.99 (3H, m).

Methyl (αξ)-α-[(ξ)-2-Methylenecyclopentyl]-β-oxo-1-(phenylsulfonyl)-1*H*-pyrrole-3-propanoate (16b) In a similar manner, **15b** (260 mg, 0.668 mmol) was oxidized with MnO_2 (872 mg, 10.0 mmol) to yield **16b** (229 mg, 89%) as a colorless syrup. HRMS Calcd for $C_{20}H_{21}NO_5S$: 387.1140. Found: 387.1127. MS *m/z*: 387 (M^+, 2), 328 (2), 307 (3), 246 (7), 234 (72), 141 (29), 77 (100), 51 (19). IR ($CHCl_3$) cm^{-1}: 1741, 1680. ^{1}H-NMR of two diastereomers (*ca.* 1 : 1) δ: 1.06—2.03 (4H, m), 2.19—2.47 (2H, m), 3.13—3.52 (1H, m), 3.62 (3H, s), 3.99 and 4.06 (1H, d each, *J* = 10 and 9.5 Hz), 4.52—4.63, 4.70—4.83 and 4.83—4.95 (2H, m each), 6.72 (1H, dd, *J* = 3.5, 1.5 Hz), 7.13 (1H, *J* = 3.5, 2 Hz), 7.41—7.76 (3H, m), 7.80—8.03 (2H, m), 7.87 (1H, dd, *J* = 2, 1.5 Hz).

3-(2ξ)-2-[(ξ)-2-Methylenecyclopentyl]-1-oxo]propyl-1-(phenylsulfonyl)-1*H*-pyrrole (17a) LiCl (184 mg, 4.33 mmol) and H_2O (78 μl, 4.3 mmol) were added successively to a solution of **16a** (90 mg, 0.22 mmol) in hexamethylphosphoramide (HMPA) (3 ml) and the mixture was heated with stirring at 130—135 °C for 14 h. H_2O was added, then the whole was extracted with Et_2O, and worked up as usual. Purification by PTLC [hexane–benzene (2 : 5)] gave **17a** (52 mg, 70%) as a colorless syrup, together with recovered **16a** (4 mg, 4%). HRMS Calcd for $C_{19}H_{21}NO_3S$: 343.1241. Found: 343.1243. MS *m/z*: 343 (M^+, 10), 287 (21), 263 (29), 234 (100), 141 (67), 77 (98). IR ($CHCl_3$) cm^{-1}: 1671. ^{1}H-NMR of *ca.* 1 : 1 mixture of diastereomers δ: 1.06 and 1.16 (3H, d each, *J* = 7 Hz), *ca.* 1.16—2.03 (4H, m), 2.03—2.47 (2H, m), 2.53—3.01 (1H, m), 3.07 and 3.22 (1H, dq each, *J* = 7, 7 Hz), 4.61—4.76 and 4.76—4.97 (2H, m each), 6.68 (1H, dd, *J* = 3.5, 1.5 Hz), 7.12 (1H, dd, *J* = 3.5, 2.5 Hz), *ca.* 7.38—7.81 (4H, m), 7.81—8.03 (2H, m).

3-[2-(2-Methylenecyclopentyl)-1-oxo]ethyl-1-(phenylsulfonyl)-1*H*-pyrrole (17b) An HMPA solution (2 ml) of **16b** (42 mg, 0.11 mmol) and $MgCl_2$ (155 mg, 1.63 mmol) was heated under an Ar atmosphere at 140—150 °C for 2 h. The same work-up as above gave **17b** (28 mg, 78%) as a colorless syrup. HRMS Calcd for $C_{18}H_{19}NO_3S$: 329.1085. Found: 329.1081. MS *m/z*: 329 (M^+, 4), 249 (14), 234 (100), 141 (37), 77 (93), 51 (19). IR ($CHCl_3$) cm^{-1}: 1679. ^{1}H-NMR δ: 0.99—2.18 (4H, m), 2.18—2.48 (2H, m), 2.65 (1H, dd, *J* = 16, 10 Hz), 2.70—3.03 (1H, m), 2.97 (1H, dd, *J* = 16, 4 Hz), 4.66—4.83 (1H, m), 4.78—4.95 (1H, m), 6.66 (1H, dd, *J* = 3.5, 1.5 Hz), 7.12 (1H, dd, *J* = 3.5, 2 Hz), 7.39—7.68 (3H, m), 7.71 (1H, dd, *J* = 2, 1.5 Hz), 7.80—8.02 (2H, m).

(αξ)-α-Butyl-α-[(1ξ)-1-[(ξ)-2-methylenecyclopentyl]ethyl]-1-(phenylsulfonyl)-1*H*-pyrrole-3-methanol (18a) A 15% *n*-BuLi solution in hexane (0.16 ml, 0.25 mmol) was added to a cooled (−75 °C) solution of **17a** (17 mg, 0.050 mmol) in THF (2 ml) under an Ar atmosphere, and stirring was continued for 10 min. Saturated NH_4Cl–H_2O was added, then the mixture was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [hexane–EtOAc (4 : 1)] afforded **18a** (10 mg, 50%) as a colorless syrup. HRMS Calcd for $C_{23}H_{31}NO_3S$: 401.2023. Found: 401.2041. MS *m/z*: 401 (M^+, 2), 383 (3), 292 (100), 234 (23), 152 (28), 109 (24), 85 (84), 77 (90), 57 (88). IR ($CHCl_3$) cm^{-1}: 1647. ^{1}H-NMR δ: 4.55—4.95 (2H, m), 6.06—6.20 (1H, m), 6.97—7.19 (2H, m), 7.30—7.70 (3H, m), 7.70—7.92 (2H, m).

(αξ)-α-[(1ξ)-1-[(ξ)-2-Methylenecyclopentyl]ethyl]-1-(phenylsulfonyl)-α-[(phenylsulfonyl)methyl]-1*H*-pyrrole-3-methanol (18b) A THF solution (3 ml) of $PhSO_2Me$ (77 mg, 0.49 mmol) was treated with 15% *n*-BuLi in hexane (0.31 ml, 0.48 mmol) at −80—−72 °C for 20 min and at −20 °C for 10 min under an Ar atmosphere, and then cooled to −80 °C. A solution of **17a** (56 mg, 0.16 mmol) in THF (2 ml) was added to this and stirring was continued at −80—−75 °C for 20 min. Saturated NH_4Cl–H_2O was added, then the mixture was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [benzene–EtOAc (19 : 1)] afforded **18b** (73 mg, 90%) as a colorless syrup. HRMS Calcd for $C_{26}H_{29}NO_5S_2$: 499.1485. Found: 499.1492. MS *m/z*: 499 (M^+, 0.3), 390 (17), 234 (34), 208 (19), 141 (51), 77 (100), 51 (23). IR ($CHCl_3$) cm^{-1}: 1646. ^{1}H-NMR δ: 0.88 (3H, d, *J* = 7 Hz), 3.41—3.89 (2H, m), 4.37—5.00 (3H including one OH, m), 5.54—5.72 (1H, m), 6.62—6.77 (1H, m), 6.96—7.12 (1H, m).

(αξ)-α-Ethyl-α-[(ξ)-2-methylenecyclopentyl]methyl-1-(phenylsuflonyl)-1*H*-pyrrole-3-methanol (18c) A solution of **17b** (33 mg, 0.10 mmol) in THF (2.5 ml) was stirred with 0.5 M EtMgBr in THF (1.20 ml, 0.60 mmol)

at 0 °C for 15 min under an Ar atmosphere. Saturated NH_4Cl–H_2O was added, then the mixture was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [benzene–EtOAc (14 : 1)] afforded **18c** (32 mg, 89%) as a colorless syrup. HRMS Calcd for $C_{20}H_{25}NO_3S$: 359.1555. Found: 359.1552. MS *m/z*: 359 (M^+, 2), 341 (7), 264 (48), 234 (40), 200 (22), 81 (44), 77 (100), 57 (78). IR ($CHCl_3$) cm^{-1}: 1648. ^{1}H-NMR δ: 0.70 and 0.73 (3H, t each, J=7.5 Hz), 4.55—4.87 (2H, m), 6.08—6.22 (1H, m), 6.98—7.17 (2H, m), 7.30—7.68 (3H, m), 7.72—7.92 (2H, m).

(αξ)-α-[(ξ)-2-Methylenecyclopentyl]methyl-1-(phenylsulfonyl)-α-[(phenylsulfonyl)methyl]-1*H*-pyrrole-3-methanol (18d) In the same manner as described for the preparation of **18b**, **17b** (32 mg, 0.097 mmol) was treated with lithiomethyl phenyl sulfone prepared from $PhSO_2Me$ (46 mg, 0.30 mmol) and 15% *n*-BuLi in hexane (0.18 ml, 0.28 mmol) to give **18d** (46 mg, 98%) as a colorless amorphous powder. MS *m/z*: 390 (5), 329 (4), 326 (5), 250 (13), 234 (63), 141 (37), 77 (100), 51 (22). ^{1}H-NMR δ: 3.49 (1H, d, J=13 Hz), 3.63 (1H, d, J=13 Hz), 4.39—4.88 (2H, m), 4.50 and 4.62 (1H, s each, OH), 5.61—5.79 (1H, m), 6.71—6.87 (1H, m), 7.00—7.15 (1H, m), 7.19—7.71 (8H, m), 7.71—8.02 (2H, m).

(αξ)-α-Butyl-α-[(1ξ)-1-[(ξ)-2-oxocyclopentyl]ethyl]-1-(phenylsulfonyl)-1*H*-pyrrole-3-methanol (19a) A solution of $NaIO_4$ (37 mg, 0.17 mmol) in H_2O (1.5 ml) was added to a solution of **18a** (14 mg, 0.035 mmol) and OsO_4 (0.5 mg, 2.0 μmol) in THF (3 ml), and the mixture was stirred at room temperature for 14 h. Saturated $Na_2S_2O_3$–H_2O was added, then the whole was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [hexane–EtOAc (3 : 1)] afforded **19a** (10 mg, 71%) as a colorless syrup. HRMS Calcd for $C_{22}N_{29}NO_4S$: 403.1816. Found: 403.1810. MS *m/z*: 403 (M^+, 2), 385 (5), 346 (43), 292 (93), 139 (65), 77 (100). IR ($CHCl_3$) cm^{-1}: 1718. ^{1}H-NMR δ: 2.47 (1H, br s, OH), 5.96—6.08 and 6.16—6.29 (total 1H, m each), 6.94—7.16 (2H, m), 7.31—7.68 (3H, m), 7.71—7.91 (2H, m).

(αξ)-α-[(1ξ)-1-[(ξ)-2-Oxocyclopentyl]ethyl]-1-(phenylsulfonyl)-α-[(phenylsulfonyl)methyl]-1*H*-pyrrole-3-methanol (19b) Similarly **19b** (31 mg, 72%) was obtained from **18b** (43 mg, 0.086 mmol) as a colorless syrup. HRMS Calcd for $C_{25}H_{27}NO_6S_2$: 501.1278. Found: 501.1269. MS *m/z*: 501 (M^+, 2), 390 (31), 234 (28), 208 (17), 141 (37),77 (100), 51 (32). IR ($CHCl_3$) cm^{-1}: 1720. ^{1}H-NMR δ: 0.91 and 0.96 (total 3H, d each, J=7 Hz), 3.44 and 3.47 (total 1H, d each, J=14 and 14.5 Hz), 3.96 and 3.73 (total 1H, d each, J=14 and 14.5 Hz), 3.93 and 5.64 (total 1H, s each, OH), 5.94—6.07 (1H, m).

(αξ)-α-Ethyl-α-[(ξ)-2-oxocyclopentyl]methyl-1-(phenylsulfonyl)-1*H*-pyrrole-3-methanol (19c) Similarly, **19c** (23 mg, 76%) was obtained as a colorless syrup from **18c** (30 mg, 0.084 mmol). HRMS Calcd for $C_{19}H_{23}NO_4S$: 361.1347. Found: 361.1327. MS *m/z*: 361 (M^+, 1), 343 (12), 332 (29), 264 (25), 234 (20), 141 (17), 125 (79), 77 (100), 57 (33), 41 (33). IR ($CHCl_3$) cm^{-1}: 1721. ^{1}H-NMR δ: 0.68 and 0.71 (3H, t each, J=7 Hz), 2.72 and 4.53 (1H, br s each, OH), 6.06 and 6.17 (1H, dd each, J=3, 2 Hz), 6.98—7.21 (2H, m), 7.33—7.71 (3H, m), 7.71—7.93 (2H, m).

(αξ)-α-[(ξ)-2-Oxocyclopentyl]methyl-1-(phenylsulfonyl)-α-[(phenylsulfonyl)methyl]-1*H*-pyrrole-3-methanol (19d) Similarly, **19d** (33 mg, 71%) was obtained as a coloress syrup from **18d** (46 mg, 0.095 mmol). MS *m/z*: 390 (3), 331 (12), 288 (11), 249 (15), 234 (47), 141 (36), 77 (100), 51 (24). IR ($CHCl_3$) cm^{-1}: 1735. ^{1}H-NMR δ: 3.55 and 3.71 (2H, s each), 4.69 and 5.20 (1H, s each, OH), 5.74—5.91 and 5.99—6.19 (1H, m each), 6.76—6.97 (1H, m), 7.00—7.18 (1H, m).

4-Butyl-5-methyl-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (20a) (i) 6% H_2SO_4-Catalyzed Reaction on 19a A solution of **19a** (9 mg, 0.022 mmol) in 6% H_2SO_4–2-propanol (2 ml) was refluxed for 1 h. Water was added, the mixture was extracted with CH_2Cl_2, then the extract was washed with saturated $NaHCO_3$–H_2O, and worked up as usual. Purification by PTLC [hexane–EtOAc (6 : 1)] gave **20a** (5.5 mg, 67%) and 4-hydroxy-5-methyl-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (**20b**) (1.5 mg, 21%) in order of increasing polarity. **20a**: Colorless syrup. HRMS Calcd for $C_{22}H_{25}NO_2S$: 367.1605. Found: 367.1597. MS *m/z*: 367 (M^+, 47), 324 (15), 184 (100), 141 (7), 77 (37), 51 (11). ^{1}H-NMR δ: 0.93 (3H, dif. t, J=6.5 Hz), *ca.* 1.23—1.71 (4H, m), 1.97 (2H, tt, J=7.5, 7.5 Hz), 2.22 (3H, s), 2.78 (2H, t, J=7 Hz), 2.83 (2H, t, J=7.5 Hz), 3.16 (2H, t, J=7.5 Hz), 6.67 (1H, d, J=4 Hz), 7.21—7.55 (3H, m), 7.55—7.79 (3H, m). **20b**: Unstable colorless syrup. HRMS Calcd for $C_{18}H_{17}NO_3S$: 327.0928. Found: 327.0922. MS *m/z*: 327 (M^+, 26), 186 (100), 171 (30), 77 (58), 51 (32). ^{1}H-NMR δ: 1.98 (2H, tt, J=7, 7 Hz), 2.16 (3H, s), 2.81 (2H, t, J=7 Hz), 3.13 (2H, t, J=7 Hz), 4.70 (1H, br s, OH), 6.69 (1H, d, J=4 Hz), 7.22—7.77 (5H, m), 7.53 (1H, d, J=4 Hz).

ii) *p*-TsOH-Catalyzed Reaction of 19a in the Presence of $PhCH_2SH$ A solution of **19a** (17 mg, 0.042 mmol) in benzene (3 ml) containing $PhCH_2SH$ (15 μl, 0.13 mmol) and *p*-TsOH·H_2O (4 mg, 0.021 mmol) was refluxed for 30 min. Saturated $NaHCO_3$–H_2O was added, then the mixture was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [hexane–EtOAc (9 : 1)] gave **20a** (14.5 mg, 94%).

5-Methyl-1-(phenylsulfonyl)-4-[(phenylsulfonyl)methyl]-1,6,7,8-tetrahydrocyclopent[*g*]indole (20c) Similarly, refluxing a benzene solution (3 ml) of **19b** (45 mg, 0.090 mmol), $PhCH_2SH$ (31 μl, 0.27 mmol), and *p*-TsOH·H_2O (8 mg, 0.042 mmol) for 2 h afforded **20c** (39 mg, 93%) as a colorless syrup after purification by PTLC (CH_2Cl_2). HRMS Calcd for $C_{25}H_{23}NO_4S_2$: 465.1067. Found: 465.1086. MS *m/z*: 465 (M^+, 10), 324 (100), 184 (42), 183 (42), 77 (62), 51 (15). ^{1}H-NMR δ: 1.99 (2H, tt, J=7.5, 7.5 Hz), 2.12 (3H, s), 2.82 (2H, t, J=7.5 Hz), 3.20 (2H, t, J=7.5 Hz), 4.61 (2H, s), 6.35 (1H, d, J=4 Hz), 7.19—7.77 (11H, m).

4-Ethyl-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (20d) i) Prepared from 19c In the same manner as above, **19c** (23 mg, 0.064 mmol) was cyclized to **20d** (19 mg, 92%) as a colorless syrup. HRMS Calcd for $C_{19}H_{19}NO_2S$: 325.1136. Found: 325.1131. MS *m/z*: 325 (M^+, 42), 184 (100), 155 (21), 77 (17), 51 (9). Other spectral data have already been reported.[23]

ii) Prepared from 20e A solution of **20e** (26 mg, 0.058 mmol) in CH_2Cl_2 (3 ml) was stirred with 15% Me_3Al in hexane (0.34 ml, 0.47 mmol) under an Ar atmosphere at 0 °C for 1 h. Saturated NH_4Cl–H_2O was added, then the mixture was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [hexane–EtOAc (19 : 1)] afforded **20d** (16.5 mg, 88%).

4-Ethyl-1-(phenylsulfonyl)-1*H*-indole (36) Refluxing a CH_2Cl_2 solution (4 ml) of **34** (45 mg, 0.109 mmol) and 15% Me_3Al in hexane (0.64 ml, 0.879 mmol) under an Ar atmosphere for 20 h, followed by the same work-up as above afforded **36** (22 mg, 71%) with recovery of **34** (9 mg, 20%) after separation by PTLC [hexane–EtOAc (6 : 1)]. **36**: Colorless needles, mp 74—75 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91. Found: C, 67.33; H, 5.39; N, 4.95. HRMS Calcd for $C_{16}H_{15}NO_2S$: 285.0823. Found: 285.0828. MS *m/z*: 285 (M^+, 48), 270 (7), 144 (100), 115 (16), 77 (33), 51 (17). ^{1}H-NMR δ: 1.23 (3H, t, J=7.5 Hz), 2.79 (2H, q, J=7.5 Hz), 6.68 (1H, d, J=4 Hz), 7.01 (1H, d, J=7.5 Hz), 7.21 (1H, dd, J=7.5, 7.5 Hz), *ca.* 7.21—7.53 (3H, m), 7.53 (1H, d, J=4 Hz), 7.72—8.01 (3H, m).

4-Ethyl-5-methyl-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]-indole (37) Similar treatment of **20c** (18 mg, 0.039 mmol) with 15% Me_3Al in hexane (0.23 ml, 0.316 mmol) at room temperature for 1 h gave **37** (11 mg, 84%) as a colorless syrup after purification by PTLC [hexane–EtOAc (24 : 1)]. HRMS Calcd for $C_{20}H_{21}NO_2S$: 339.1293. Found: 339.1302. MS *m/z*: 339 (M^+, 42), 198 (100), 169 (18), 77 (28), 51 (14). ^{1}H-NMR δ: 1.15 (3H, t, J=7.5 Hz), 1.97 (2H, tt, J=7.5, 7.5 Hz), 2.23 (3H, s), 2.82 (2H, q, J=7.5 Hz), 2.84 (2H, t, J=7.5 Hz), 3.18 (2H, t, J=7.5 Hz), 6.69 (1H, d, J=4 Hz), 7.26—7.54 (3H, m), 7.54—7.79 (2H, m), 7.62 (1H, d, J=4 Hz).

1-(Phenylsulfonyl)-4-[(phenylsulfonyl)methyl]-1,6,7,8-tetrahydrocyclopent[*g*]indole (20e) Similarly, the acid-catalyzed cyclization of **19d** (33 mg, 0.068 mmol) afforded **20e** (27.5 mg, 90%) as a colorless glass. HRMS Calcd for $C_{24}H_{21}NO_4S_2$: 451.0912. Found: 451.0918. MS *m/z*: 451 (M^+, 6), 310 (100), 169 (32), 77 (25), 51 (9). ^{1}H-NMR δ: 1.96 (2H, tt, J=7.5, 7.5 Hz), 2.83 (2H, t, J=7.5 Hz), 3.13 (2H, t, J=7.5 Hz), 4.46 (2H, s), 6.37 (1H, d, J=4 Hz), 7.17—7.76 (11H, m), 7.53 (1H, d, J=4 Hz).

4-*n*-Butyl-5-methyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (25) A solution of **20a** (13 mg, 0.035 mmol) in 20% KOH in DME–MeOH–H_2O (1 : 1 : 1) (2.1 ml) was refluxed for 6 h. Saturated NH_4Cl–H_2O was added at 0 °C, then the mixture was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [hexane–EtOAc (19 : 1)] afforded **25** (7.5 mg, 93%) as a colorless syrup, which turned purple on storage. HRMS Calcd for $C_{16}H_{21}N$: 227.1674. Found: 227.1671. MS *m/z*: 227 (M^+, 35), 184 (100). ^{1}H-NMR δ: 0.94 (3H, dif. t, J=7 Hz), 1.23—1.81 (4H, m), 2.17 (2H, tt, J=7, 7 Hz), 2.29 (3H, s), 2.73—3.17 (6H, m), 6.52 (1H, dd, J=3, 2 Hz), 7.06 (1H, dd, J=3, 3 Hz), 7.82 (1H, br s, NH).

5-Methyl-4-[(phenylsulfonyl)methyl]-1,6,7,8-tetrahydrocyclopent[*g*]-indole (26a) A solution of **20c** (30 mg, 0.065 mmol) in 10% NaOH in DME–MeOH–H_2O (2 : 1 : 1) (4 ml) was refluxed for 4 h. Saturated NH_4Cl–H_2O was added at 0 °C, then the mixture was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [hexane–EtOAc (7 : 1)] afforded 5-methyl-4-[(methoxy)methyl]-1,6,7,8-tetrahydrocyclopent[*g*]indole (**26b**) (7.5 mg, 54%) and crude **26a**. The latter was further purified by PTLC [hexane–CH_2Cl_2 (1 : 2)] to yield **26a** (7 mg, 33%) as a colorless syrup. HRMS Calcd for $C_{19}H_{19}NO_2S$: 325.1136. Found:

325.1134. MS *m/z*: 325 (M^+, 6), 184 (100), 77 (23), 51 (13). ^{1}H-NMR δ: 2.11 (3H, s), 2.17 (2H, tt, J=7.5, 7.5 Hz), 2.91 (2H, t, J=7.5 Hz), 3.04 (2H, t, J=7.5 Hz), 4.71 (2H, s),6.14—6.29 (1H, m), 6.94—7.08 (1H, m), *ca.* 7.21—7.60 (3H, m), 7.60—7.81 (2H, m), 7.91 (1H, br s, NH). **26b**: Colorless syrup. HRMS Calcd for $C_{14}H_{17}NO$: 215.1310. Found: 215.1310. MS *m/z*: 215 (M^+, 79), 200 (14), 184 (100). ^{1}H-NMR δ: 2.18 (2H, tt, J=7, 7 Hz), 2.37 (3H, s), 2.80—3.17 (4H, m), 3.39 (3H, s), 4.79 (2H, s), 6.63 (1H, dd, J=3, 2 Hz), 7.09 (1H, dd, J=3, 3 Hz), 7.93 (1H, br s, NH).

4,5-Dimethyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (27) Mg (79 mg, 3.3 mg atm) and NH_4Cl (7 mg, 0.13 mmol) were added to a solution of **20c** (30 mg, 0.065 mmol) in MeOH (5 ml) and the mixture was stirred at room temperature for 2 h. Saturated NH_4Cl–H_2O was added, then the whole was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [hexane–CH_2Cl_2 (3 : 1)] gave **27** (11 mg, 92%) as colorless needles, mp 150.5—151 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.41; H, 8.26; N, 7.49. HRMS Calcd for $C_{13}H_{15}N$: 185.1204. Found: 185.1204. MS *m/z*: 185 (M^+, 100), 170 (73). ^{1}H-NMR δ: 2.17 (2H, tt, J=7, 7 Hz), 2.27 (3H, s), 2.46 (3H, s), 2.86—3.18 (4H, m), 6.52 (1H, dd, J=3, 2 Hz, changed with D_2O to d, J=3 Hz), 7.09 (1H, dd, J=3, 3 Hz, changed with D_2O to d, J=3 Hz), 7.84 (1H, br s, disappeared with D_2O).

4-(3-Butenyl)-5-methyl-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (30a) Allyltrimethylsilane (38 μl, 0.24 mmol) and 0.95 M $EtAlCl_2$ in hexane (0.17 ml, 0.16 mmol) were successively added to a solution of **20c** (18.5 mg, 0.040 mmol) in CH_2Cl_2 (2 ml) at −20 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 30 min. Saturated $NaHCO_3$–H_2O was added, then the whole was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [hexane–EtOAc (9 : 1)] afforded **30a** (13 mg, 90%) as a colorless syrup. HRMS Calcd for $C_{22}H_{23}NO_2S$: 365.1448. Found: 365.1440. MS *m/z*: 365 (M^+, 31), 324 (100), 224 (12), 183 (30), 168 (20), 167 (20), 77 (48), 51 (18). IR ($CHCl_3$) cm^{-1}: 1640. ^{1}H-NMR δ: 1.98 (2H, tt, J=7.5, 7.5 Hz), 2.10—2.44 (2H, m), 2.23 (3H, s), 2.84 (2H, t, J=7.5 Hz), 2.90 (2H, t, J=8 Hz), 3.17 (2H, t, J=7.5 Hz), 4.96 (1H, dd, J=10, 2 Hz), 5.04 (1H, dd, J=17, 2 Hz), 5.88 (1H, ddt, J=17, 10, 6.5 Hz), 6.68 (1H, d, J=4 Hz), 7.26—7.56 (3H, m), 7.56—7.80 (3H, m), 7.63 (1H, d, J=4 Hz).

4-(3-Butenyl)-1-(phenylsulfonyl)-1*H*-indole (35) In a similar manner, **34** (57 mg, 0.14 mmol) was treated with allyltrimethylsilane (176 μl, 1.1 mmol) and 0.95 M $EtAlCl_2$ in hexane (0.73 ml, 0.69 mmol) in CH_2Cl_2 (3 ml) at −20 °C for 3 h. The same work-up as above, followed by PTLC [hexane–EtOAc (5 : 1)] afforded **35** (34 mg, 79%) as a colorless oil. HRMS Calcd for $C_{18}H_{17}NO_2S$: 311.0980. Found: 311.0985. MS *m/z*: 311 (M^+, 31), 270 (100), 129 (26), 102 (15), 77 (62), 51 (21). IR ($CHCl_3$) cm^{-1}: 1639. ^{1}H-NMR δ: 2.20—2.55 (2H, m), 2.86 (2H, dd, J=8.5, 5.5 Hz), 4.93 (1H, br d, J=9.5 Hz), 4.99 (1H, br d, J=17 Hz), 5.83 (1H, ddt, J=17, 9.5, 6.5 Hz), 6.69 (1H, d, J=4 Hz), 7.02 (1H, d, J=7.5 Hz), 7.22 (1H, dd, J=7.5, 7.5 Hz), *ca.* 7.22—7.54 (3H, m), 7.54 (1H, d, J=4 Hz), 7.73—7.99 (2H, m), 7.87 (1H, d, J=7.5 Hz).

4-(3-Butenyl)-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (30b) Similarly, **30b** (12 mg, 86%) was obtained as a colorless syrup by treatment of **20e** (18 mg, 0.040 mmol) with allyltrimethylsilane (38 μl, 0.24 mmol) and 0.95 M $EtAlCl_2$ in hexane (0.17 ml, 0.16 mmol) under an Ar atmopshere at −20 °C for 15 min. HRMS Calcd for $C_{21}H_{21}NO_2S$: 351.1292. Found: 351.1306. MS *m/z*: 351 (M^+, 28), 310 (100), 168 (29), 77 (42), 51 (14), 43 (18). IR ($CHCl_3$) cm^{-1}: 1640. ^{1}H-NMR δ: 1.97 (2H, tt, J=7.5, 7.5 Hz), 2.23—2.59 (2H, m), 2.72—3.03 (4H, m), 3.14 (2H, t, J=7.5 Hz), 4.96 (1H, ddt, J=10, 2, 1 Hz), 5.03 (1H, ddt, J=17, 2, 1.5 Hz), 5.87 (1H, ddt, J=17, 10, 6 Hz), 6.71 (1H, d, J=4 Hz), 6.98 (1H, s), 7.27—7.57 (3H, m), 7.57—7.81 (2H, m), 7.66 (1H, d, J=4 Hz).

4-[(*E*)-1-Butenyl]-5-methyl-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (32a) A solution of **30a** (18 mg, 0.049 mmol) in EtOH (1.5 ml) containing $RhCl_3 \cdot 3H_2O$ (1 mg, 4 μmol) was heated in a sealed tube under an Ar atmosphere at 100 °C for 50 h. Saturated $NaHCO_3$–H_2O was added at 0 °C, then the mixure was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [Merck SiO_2 $60F_{254}$ (20 × 20) plate, hexane–EtOAc (49 : 1)] afforded **32a** (12 mg, 67%) along with **31** (4 mg, 22%). **32a**: Colorless prisms, mp 118—119 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{22}H_{23}NO_2S$: C, 72.29; H, 6.34; N, 3.83. Found: C, 72.21; H, 6.43; N, 3.75. HRMS Calcd for $C_{22}H_{23}NO_2S$: 365.1448. Found: 365.1441. MS *m/z*: 365 (M^+, 64), 224 (100), 209 (16), 208 (16), 197 (35), 77 (65), 51 (26). ^{1}H-NMR δ: 1.11 (3H, t, J=7 Hz), 1.97 (2H, tt, J=7.5, 7.5 Hz), 2.21 (3H, s), 2.26 (2H, dq, J=6.5, 7 Hz), 2.83 (2H, t, J=7.5 Hz), 3.18 (2H, t, J=7.5 Hz), 5.91 (1H, dt, J=16, 6.5 Hz), 6.55 (1H, d, J=16 Hz), 6.78 (1H, d, J=4 Hz), 7.21—7.54 (3H, m), 7.54—7.79 (2H, m), 7.58 (1H, d, J=4 Hz). 4-(2-Butenyl)-5-methyl-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (**31**): Colorless syrup. HRMS Calcd for $C_{22}H_{23}NO_2S$: 365.1448. Found: 365.1442. MS *m/z*: 365 (M^+, 99), 224 (100), 209 (50), 77 (93), 51 (38). ^{1}H-NMR of major and minor isomers δ: 1.59 and 1.78 (3H, br d each, J=5.5 Hz), 1.97 (2H, tt, J=7.5, 7.5 Hz), 2.21 (3H, s), 2.84 (2H, t, J=7.5 Hz), 3.17 (2H, t, J=7.5 Hz), 3.38—3.66 (2H, m), 5.18—5.69 (2H, m), 6.68 and 6.79 (1H, d each, J=4 Hz), 7.22—7.54 (3H, m), 7.54—7.79 (2H, m).

4-[(*E*)-1-Butenyl]-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (32b) An EtOH solution (0.5 ml) of **30b** (11 mg, 0.031 mmol) containing $RhCl_3 \cdot 3H_2O$ (0.5 mg, 2 μmol) was refluxed under an Ar atmosphere for 8 h. Similar work-up to the above, followed by purification by PTLC [hexane–EtOAc (19 : 1)], afforded **32b** (9 mg, 82%) as a colorless syrup. HRMS Calcd for $C_{21}H_{21}NO_2S$: 351.1292. Found: 351.1289. MS *m/z*: 351 (M^+, 67), 210 (100), 183 (29), 167 (18), 77 (36), 51 (14). ^{1}H-NMR δ: 1.09 (3H, t, J=7 Hz), 1.97 (2H, tt, J=7.5, 7.5 Hz), 2.26 (2H, dq, J=6.5, 7 Hz), 2.89 (2H, t, J=7.5 Hz), 3.13 (2H, t, J=7.5 Hz), 6.24 (1H, dt, J=16, 6.5 Hz), 6.66 (1H, d, J=16 Hz), 6.81 (1H, d, J=4 Hz), 7.22 (1H, s), *ca.* 7.22—7.55 (3H, m), 7.55—7.77 (2H, m), 7.64 (1H, d, J=4 Hz).

4-[(*E*)-1-Butenyl]-5-methyl-1,6,7,8-tetrahydrocyclopent[*g*]indole (33) In the same manner as described for the preparation of **25**, **32a** (8 mg, 0.022 mmol) was hydrolyzed to yield **33** (4.5 mg, 91%) as a colorless syrup. HRMS Calcd for $C_{16}H_{19}N$: 225.1517. Found: 225.1533. MS *m/z*: 225 (M^+, 100), 210 (64), 195 (25), 184 (18), 167 (15), 138 (10). ^{1}H-NMR δ: 1.14 (3H, t, J=7.5 Hz), 1.97—2.50 (4H, m), 2.31 (3H, s), 2.82—3.16 (4H, m), 6.12 (1H, dt, J=16, 6.5 Hz), 6.64 (1H, dd, J=3, 2 Hz), 6.71 (1H, br d, J=16 Hz), 7.06 (1H, dd, J=3, 3 Hz), 7.83 (1H, br s, NH).

Methyl(α*ξ*,β*ξ*)-β-Hydroxy-α-[(*ξ*)-2-oxocyclopentyl]-1-(phenylsulfonyl)-1*H*-pyrrole-3-propanoate (38) In the same manner as described for the preparation of **19a**, **15b** (87 mg, 0.22 mmol) was treated with OsO_4 (2 mg, 8 μmol) and $NaIO_4$ (192 mg, 0.90 mmol) in THF–H_2O (3 : 1) (4 ml) at room temperature for 18 h to afford **38** (68 mg, 78%) as a colorless syrup. HRMS Calcd for $C_{19}H_{21}NO_6S$: 391.1089. Found: 391.1103. MS *m/z*: 391 (M^+, 0.2), 373 (0.6), 308 (1), 250 (2), 141 (17), 77 (100), 55 (11). IR ($CHCl_3$) cm^{-1}: 1732. ^{1}H-NMR δ: 3.64 (3H, s), 6.08—6.19 and 6.23—6.39 (1H, m each), 7.01—7.23 (2H, m), 7.32—7.70 (3H, m), 7.70—7.98 (2H, m).

Methyl 1-(Phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole-5-carboxylate (39) A benzene solution (5 ml) of **38** (151 mg, 0.386 mmol) containing PhSH (158 μl, 1.54 mmol) and *p*-TsOH·H_2O (18 mg, 0.095 mmol) was refluxed for 2 h. The same work-up as for **20a**, followed by purification by PTLC [hexane–CH_2Cl_2 (2 : 1)] afforded **39** (110 mg, 80%) as colorless needles, mp 182—183 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{19}H_{17}NO_4S$: C, 64.21; H, 4.82; N, 3.94. Found: C, 64.14; H, 4.83; N, 3.92. HRMS Calcd for $C_{19}H_{17}NO_4S$: 355.0877. Found: 355.0874. MS *m/z*: 355 (M^+, 72), 214 (79), 182 (100), 154 (95), 77 (91), 51 (52). IR (KBr) cm^{-1}: 1704. ^{1}H-NMR δ: 1.99 (2H, tt, J=7.5, 7.5 Hz), 3.18 (2H, t, J=7.5 Hz), 3.27 (2H, t, J=7.5 Hz), 3.86 (3H, s), 6.72 (1H, d, J=4 Hz), 7.29—7.59 (3H, m), 7.59—7.81 (2H, m), 7.72 (1H, d, J=4 Hz), 8.08 (1H, s).

5-(Hydroxymethyl)-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (40) $LiAlH_4$ (7 mg, 0.18 mmol) was added to a solution of **39** (23 mg, 0.065 mmol) in THF (2.5 ml) under an Ar atmosphere at −20 °C, and the mixture was stirred at the same temperature for 1 h. Saturated Rochelle salt–H_2O was added, then the whole was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [hexane–EtOAc (2 : 1)] gave **40** (20 mg, 94%) as colorless needles, mp 125—126 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.23; N, 4.28. Found: C, 66.24; H, 5.23; N, 4.32. HRMS Calcd for $C_{18}H_{17}NO_3S$: 327.0929. Found: 327.0934. MS *m/z*: 327 (M^+, 36), 184 (31), 168 (100), 77 (35), 51 (20). ^{1}H-NMR δ: 1.73 (1H, br s, OH), 1.99 (2H, tt, J=7.5, 7.5 Hz), 2.88 (2H, t, J=7.5 Hz), 3.18 (2H, t, J=7.5 Hz), 4.64 (2H, s), 6.63 (1H, d, J=4 Hz), 7.24—7.54 (3H, m), 7.36 (1H, s), 7.54—7.78 (2H, m), 7.63 (1H, d, J=4 Hz).

5-Formyl-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (41) A CH_2Cl_2 slurry (6 ml) of **40** (87 mg, 0.27 mmol) and MnO_2 (347 mg, 3.99 mmol) was stirred at room temperature for 1.5 h. This was worked up as described for **16a**, and purification by PTLC [hexane–CH_2Cl_2 (1 : 1)] gave **41** (81 mg, 94%) as colorless needles, mp 174—175 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{18}H_{15}NO_3S$: C, 66.44; H, 4.65; N,

4.31. Found: C, 66.33; H, 4.64; N, 4.26. HRMS Calcd for $C_{18}H_{15}NO_3S$: 325.0772. Found: 325.0784. MS *m/z*: 325 (M^+, 22), 184 (100), 156 (20), 154 (22), 77 (32), 51 (18). IR (KBr) cm^{-1}: 1678. ^{1}H-NMR δ: 2.06 (2H, tt, J=7.5, 7.5 Hz), 3.17 (2H, t, J=7.5 Hz), 3.28 (2H, t, J=7.5 Hz), 6.79 (1H, d, J=4 Hz), 7.31—7.61 (3H, m), 7.61—7.84 (2H, m), 7.77 (1H, d, J=4 Hz), 7.87 (1H, s), 10.16 (1H, s).

5-(1-Hydroxy-1-butyl)-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent-[*g*]indole (44) A THF solution (2 ml) of **41** (35 mg, 0.11 mmol) was stirred with 0.5 M *n*-PrMgBr in THF (0.65 ml, 0.33 mmol) under an Ar atmosphere at −20 °C for 20 min. Saturated NH_4Cl–H_2O was added, then the mixture was extracted with CH_2Cl_2 and worked up as usual. Purification by PTLC (CH_2Cl_2) afforded **44** (36 mg, 91%) as colorless needles, mp 120—121 °C (CH_2Cl_2–hexane), together with **40** (3 mg, 8.5%). *Anal.* Calcd for $C_{21}H_{23}NO_3S$: C, 68.26; H, 6.27; N, 3.79. Found: C, 68.27; H, 6.32; N, 3.80. HRMS Calcd for $C_{21}H_{23}NO_3S$: 369.1398. Found: 369.1391. MS *m/z*: 369 (M^+, 38), 351 (11), 326 (100), 210 (37), 185 (34), 168 (33), 156 (82), 77 (69), 51 (28), 43 (32). ^{1}H-NMR δ: 0.89 (3H, t, J=6.5 Hz), *ca.* 1.13—1.89 (4H, m), 1.89 (1H, s, OH), 1.98 (2H, tt, J=7.5, 7.5 Hz), 2.87 (2H, t, J=7.5 Hz), 3.16 (2H, t, J=7.5 Hz), 4.80 (1H, t, J=6 Hz), 6.62 (1H, d, J=4 Hz), 7.23—7.54 (4H, m), 7.54—7.77 (2H, m), 7.61 (1H, d, J=4 Hz).

5-[(*E*)-1-Butenyl]-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]-indole (42) i) Dehydration of 44 A benzene solution (3 ml) of **44** (12 mg, 0.033 mmol) and *p*-TsOH·H_2O (1.5 mg, 0.008 mmol) was gently refluxed for 10 min. Saturated $NaHCO_3$–H_2O was added at 0 °C, then the mixture was extracted with CH_2Cl_2, and worked up as usual. Purification by PTLC [hexane–CH_2Cl_2 (2 : 1)] gave **42** (10.5 mg, 92%) as colorless prisms, mp 103—104 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{21}H_{21}NO_2S$: C, 71.76; H, 6.02; N, 3.99. Found: C, 71.70; H, 6.06; N, 4.04. HRMS Calcd for $C_{21}H_{21}NO_2S$: 351.1293. Found: 351.1306. MS *m/z*: 351 (M^+, 81), 210 (100), 168 (80), 77 (64), 51 (26). ^{1}H-NMR δ: 1.06 (3H, t, J=7.5 Hz), 1.99 (2H, tt, J=7.5, 7.5 Hz), 2.21 (2H, dq, J=6, 7.5 Hz), 2.92 (2H, t, J=7.5 Hz), 3.19 (2H, t, J=7.5 Hz), 6.11 (1H, dt, J=16, 6 Hz), 6.47 (1H, d, J=16 Hz), 6.60 (1H, d, J=4 Hz), 7.20—7.54 (3H, m), 7.54—7.78 (2H, m), 7.59 (1H, d, J=4 Hz).

ii) Wittig Reaction of 41 A slurry of *n*-propyltriphenylphosphonium bromide (166 mg, 0.43 mmol) in THF (3 ml) was treated with 1.68 M BuLi in hexane (0.26 ml, 0.41 mmol) under an Ar atmosphere at −20 °C, and the mixture was stirred at −20 °C for 30 min. A THF solution (2 ml) of **37** (35 mg, 0.11 mmol) was added dropwise to this and the whole was stirred at −20 °C for 30 min. Saturated NH_4Cl–H_2O was added, then the mixture was extracted with CH_2Cl_2, and worked up as usual. The residue (166 mg) obtained here was dissolved in THF–DMF (3 : 1) (4 ml), 60% NaH (21 mg, 0.53 mmol) was added to this, and the whole was stirred under an Ar atmosphere at room temperature for 15 h. Saturated NH_4Cl–H_2O was added, then the mixture was extracted with Et_2O, and worked up as usual. Separation by PTLC [hexane–DME (99 : 1)] afforded both **42** (12 mg, 32%), colorless prisms, mp 103—104 °C (CH_2Cl_2–hexane) as a more polar isomer and 5-[(*Z*)-1-butenyl]-1-(phenylsulfonyl)-1,6,7,8-tetrahydrocyclopent[*g*]indole (**43**) as a less polar isomer. **43**: Colorless syrup. HRMS Calcd for $C_{21}H_{21}NO_2S$: 351.1293. Found: 351.1297. MS *m/z*: 351 (M^+, 77), 210 (100), 168 (76), 77 (67), 51 (31). ^{1}H-NMR δ: 1.00 (3H, t, J=7.5 Hz), 1.99 (2H, tt, J=7.5, 7.5 Hz), 2.24 (2H, dq, J=7, 7.5 Hz), 2.82 (2H, t, J=7.5 Hz), 3.20 (2H, t, J=7.5 Hz), 5.64 (1H, dt, J=11.5, 7 Hz), 6.34 (1H, d, J=11.5 Hz), 6.64 (1H, d, J=4 Hz), 7.24 (1H, s), *ca.* 7.24—7.56 (3H, m), 7.56—7.83 (2H, m), 7.62 (1H, d, J=4 Hz).

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