Stereoselective Total Syntheses of (±)-Gymnomitrol and (±)-Gymnomitrene

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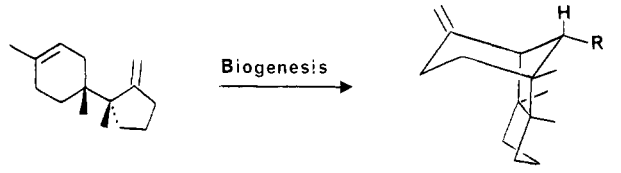
Stereoselective total syntheses of (±)-gymnomitrol (**2A**) and (±)-gymnomitrene (**2B**) in 12 synthetic stages each from 2-methylcyclopentanone (**3**) are presented. The key features of these syntheses are (a) the conjugate addition of lithium dimethylcopper to enone **8** followed by alkylation of the intermediate enolate anion with allyl chloride to afford ketone **9**, (b) stereoselective alkylation of ketone **9**, (c) a modified intramolecular Claisen condensation and enolate anion trapping with *tert*-butyldimethylsilyl chloride to give tricyclic ketone **14B**, and (d) convenient utilization of a common intermediate in the construction of both natural products **2A** and **2B** by sequential chemical manipulation of **15A** followed by desilylation to produce either ketone **16** or **18** in one-pot reactions.

The tricyclic sesquiterpenoid gymnomitrol (**2A**) was isolated as a major metabolite from liverwort *Gymnomitrion obtusum* (Lindb.) Pears.[1] The corresponding hydrocarbon, gymnomitrene (**2B**, previously known as β-barbatene[2] of β-pompene[3]), also occurs with gymnomitrol (**2A**) as well as in the leafy liverwort *Bazzania pompeana* (Lac.) Mitt. (*Hepaticae*) and other liverwort species.[2,3] The structure and stereochemistry of both natural products were determined by degradation and spectroscopy in conjunction with biogenetic considerations.[1-4] A recent X-ray analysis of the *p*-bromobenzoate monoester of the diol derived from **2B** confirms the original structural assignment as well as the absolute configuration for these naturally occurring substances.[3a] The unique carbon framework of these cyclotrichothecanes is thought to arise, biogenetically, from bazzanene (**1**, Scheme I).[1-4] We wish to report, herein, the full details of our stereoselective total syntheses of (±)-glymnomitrol (**2A**) and (±)-gymnomitrene (**2B**) via a common synthetic intermediate.[5,6]

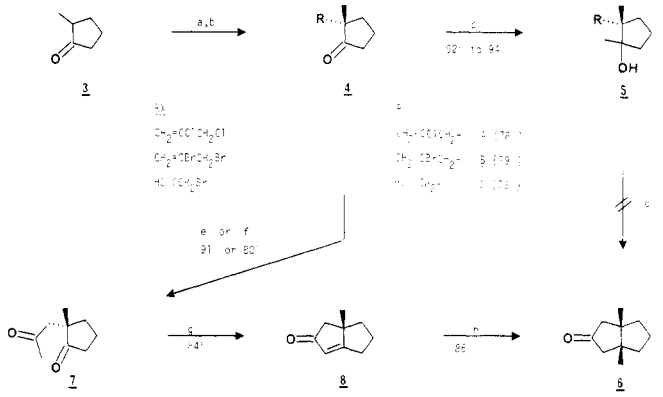
The starting material chosen for these syntheses is 2-methylcyclopentanone (**3**, Scheme II). Normally, cyclopentanones are difficult to alkylate because of the relative ease of enolization, aldol condensation, and polyalkylation.[7] A number of methods for the regioselective alkylation of unsymmetrical ketones such as 2-methylcyclopentanone (**3**) have been developed.[8-10] In practice, however, we

Scheme I



1 **2A** R = OH **2B** R = H

Scheme II. Synthesis of Pentalenone 8[a]



3 **4** **5** **7** **8** **9**

[a] (a) 0.95-0.99% LDA, THF, 0 °C to room temperature, 4 h. (b) RX. (c) CH_3Li, Et_2O. (d) CF_3CO_2H, $(CF_3CO)_2O$, $Hg(OAc)_2$. (e) 90% H_2SO_4, 0 °C or HCO_2H, $Hg(OAc)_2$, CH_2Cl_2 for **4B**. (f) HgO, H_2SO_4, H_2O, CH_2Cl_2 for **4C**. (g) KOH, EtOH or KO-*t*-Bu, *t*-BuOH. (h) $Li(CH_3)_2Cu$, Et_2O.

found that generation of the enolate anion with 0.95–0.99 equiv of lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at −78 °C, equilibration to the thermodynamically more stable enolate anion at room temperature for 1.25–1.5 h, and then quenching with either 2,3-dichloropropene, 2,3-dibromopropene, or propargyl bromide at 0 °C affords, after medium-pressure preparative liquid chromatography on silica gel, ketones **4A–C** in 73–79% yields. Use of the House enol acetate or the Stork trimethylsilyl enol ether methods resulted in substantially

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(2) Andersen, N. H.; Huneck, S. *Phytochemistry* **1973**, *12*, 1818–1819. Andersen, N. H.; Costin, C. R.; Kramer, C. M., Jr.; Ohta, Y.; Huneck, S. *Ibid.* **1973**, *12*, 2709–2716. Andersen, N. H.; Tseng, C. W.; Moore, A.; Ohta, Y. *Tetrahedron* **1978**, *34*, 47–52.

(3) Nozaki, H.; Matsuo, A.; Nakayama, M.; Kushi, Y.; Kamijo, N.; Hayashi, S. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 568–574. Matsuo, A.; Uto, S.; Nakayama, M.; Hayashi, S. *Z. Naturforsch.: Biosci.* **1976**, *31C*, 401–402. Matsuo, A.; Nozaki, H.; Nakayama, M.; Kushi, Y.; Hayashi, S.; Kamijo, N. *Tetrahedron Lett.* **1975**, 241–244. Matsuo, A.; Maeda, T.; Nakayama, M.; Hayashi, S. *Ibid.* **1973**, 4131–4134.

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(6) For reports of other syntheses in this family of natural products see: (a) Coates, R. M.; Shah, S. K.; Mason, R. W. *J. Am. Chem. Soc.* **1979**, *101*, 6765–6767; (b) Büchi, G.; Chu, P.-S. *Ibid.* **1979**, *101*, 6767–6768; (c) Han, Y.-K.; Paquette, L. A. *J. Org. Chem.* **1979**, *44*, 3731–3733; (d) Kodama, M.; Kurihara, T.; Sasaki, J.; Itô, S. *Can. J. Chem.* **1979**, *57*, 3343–3344.

(7) Caine, D. In "Carbon-Carbon Bond Formation"; Augustine, R. L., Ed.; Marcel Dekker: New York, 1979; Vol. I, pp 85–352. d'Angelo, J. *Tetrahedron* **1976**, *32*, 2979–2990. House, H. O. *Rec. Chem. Prog.* **1967**, *28*, 98–120. Conia, J.-M. *Ibid.* **1963**, *24*, 42–62.

(8) For alkylation via enol acetates, see: House, H. O.; Trost, B. M. *J. Org. Chem.* **1965**, *30*, 2502–2512.

(9) For alkylation via trimethylsilyl enol ethers, see: Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4462–4464, 4464–4465.

(10) For alkylation via the *n*-butylthiomethylene blocking group, see: Coates, R. M.; Sowerby, R. L. *J. Am. Chem. Soc.* **1971**, *93*, 1027–1029; Ireland, R. E.; Marshall, J. A. *J. Org. Chem.* **1962**, *27*, 1615–1619, 1620–1627.

(11) The ratio of the thermodynamic to kinetic lithium enolate anions of 2-methylcyclopentanone at equilibrium is 94:6, respectively, according to: House, H. O.; Trost, B. M. *J. Org. Chem.* **1965**, *30*, 1341–1352; House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; p 559.

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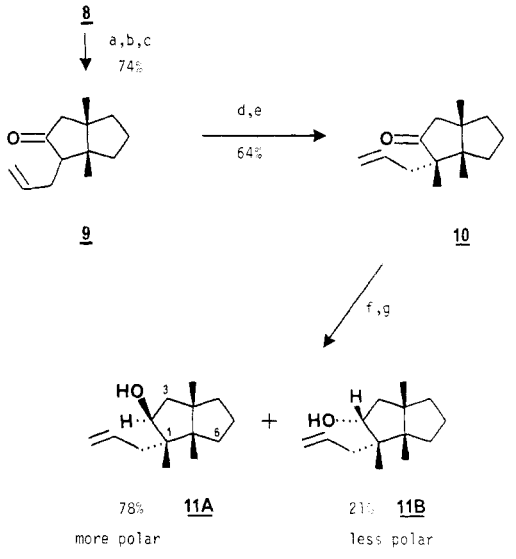
lower (~43–47%) overall yields.[8,9]

The original synthetic plan was to explore the possibility of utilizing an acid-catalyzed 5-endo-trigonal[12] ring closure of vinyl halides **5A,B** or a 5-endo-diagonal[12] cyclization of alkyne **5C** to produce cis-fused 1,5-dimethylbicyclo-[3.3.0]octan-3-one (**6**). This was to serve as a model for an intermediate which would contain a three-carbon side chain at position 2 in the resulting ketone **6**. The later three-carbon unit would then serve to construct the requisite cyclohexanone at a later stage in the synthesis. Lansbury and co-workers[13] have reported several successful cationic 5-endo-trigonal cyclizations to cyclopentanones despite the fact that Baldwin's rules[12] predict this type of ring closure to be a geometrically disfavored one. According to Baldwin's rules[12] a 5-endo-diagonal ring closure should be a sterically favored process. With this background in mind, tertiary alcohols **5A–C** were prepared in 92–94% yield from ketones **4A–C**, respectively, by treatment with methyllithium in ether. All attempts at acid-catalyzed cyclizations of alcohols **5A–C** to cyclopentanone **6** by using trifluoroacetic acid–trifluoroacetic anhydride with or without mercury(II) acetate were unsuccessful. At this point the synthetic scheme was altered to include the construction of pentalenone **8**.[14] Enone **8** would serve as an intermediate for the synchronous introduction of the angular methyl group and the three-carbon side chain via a conjugate addition–alkylation reaction sequence.[15]

Hydrolysis of vinyl bromide **4B** with 90% sulfuric acid at 0 °C proceeds smoothly in 91% yield on a small scale (200–800 mg) to give diketone **7**; however, the yields decreased dramatically on larger scale runs. To circumvent this troublesome step, we selected an alternative method. Vinyl bromide **4B** is conveniently hydrolyzed to diketone **7** in 91% yield by utilizing mercury(II) acetate in 88% formic acid–dichloromethane at room temperature.[16a] Hydrolysis of alkyne **4C** to diketone **7** was smoothly accomplished in 80% yield with mercury(II) oxide in aqueous sulfuric acid–dichloromethane at 60 °C. Cyclization of diketone **7** to bicyclic enone **8** is effected in 84% yield with potassium hydroxide in ethanol at reflux or in 77% yield with potassium *tert*-butoxide in *tert*-butyl alcohol at room temperature. Treatment of enone **8** with lithium dimethylcopper[15] in ether affords bicyclic ketone **6** in 86% yield as a single isomer. Ketone **6** had been prepared previously by alternate synthetic routes.[6a,c,17] The cis-fused bicyclo[3.3.0]octan-3-one skeleton was expected as the major product because of the large thermodynamic stability of the cis-fused vs. trans-fused isomer.[18] Alkylation of ketone **6** with LDA in THF followed by the sequential addition of hexamethylphosphoric triamide (HMPA) and allyl bromide gives ketone **9** (Scheme III) in 67% yield as a 60:40 ratio of isomers at carbon 2.

Scheme III. Synthesis and Stereochemistry of Ketone 10[a]



Europium NMR Shift Analysis

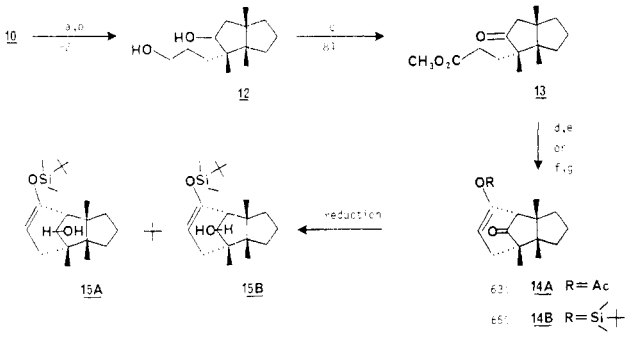
	dist, Å[b]	rel slope[c]	dist, Å[b]	rel slope[c]
C_1-Me	2.5	7.84	3.7	3.39
C_{3a}-Me	4.5	2.53	4.9	1.32
C_{6a}-Me	4.5	2.51	4.9	1.00

[a] (a) $Li(CH_3)_2Cu$, THF. (b) $ClCH_2CH{=}CH_2$, HMPA. (c) H_3O^+. (d) NaH, DME. (e) CH_3I. (f) $NaBH_4$, EtOH, 25 °C. (g) Chromatography on silica gel using 15% Et_2O/85% petroleum ether as an eluant. [b] Measured distance from the OH group using Dreiding stereomodels. [c] The slopes are calculated by plotting $\Delta\delta_{Me}$ vs. $\Delta[Eu(DPM)_3]/[ROH]$.

Addition of enone **8** to a solution of lithium dimethylcopper in THF at −78 °C followed by sequential introduction of HMPA and allyl chloride at room temperature with an aqueous ammonium chloride workup affords bicyclic ketone **9** (Scheme III) in 74% yield.[15] Alkylation of ketone **9** utilizing sodium hydride in 1,2-dimethoxyethane (DME) followed by addition of methyl iodide produces ketone **10** in 64% yield as a single diastereomer.[19,20] This alkylation takes place with the alkylating agent, methyl iodide, approaching the less hindered, convex side of the thermodynamically more stable enolate anion. The stereochemical assignment of methylation product **10** is confirmed by analysis of the europium-induced NMR shifts[21] for the three quaternary methyl groups in the two isomeric alcohols **11A,B** formed by reduction of ketone **10** with sodium borohydride in 100% ethanol. This reduction affords a 79:21 ratio of diastereomeric alcohols **11A** and **11B**, respectively, which are separated by chromatography on silica gel. The magni-

(12) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734–736.
(13) Lansbury, P. T.; Nienhouse, E. J.; Scharf, D. J.; Hilfiker, F. R. *J. Am. Chem. Soc.* **1970**, *92*, 5649–5657. Lansbury, P. T.; Nienhouse, E. J. *Ibid.* **1966**, *88*, 4290–4291.
(14) During the course of our work an alternative synthesis of bicyclic enone **8** was published by: Miyashita, M.; Yanami, T.; Yoshikoshi, A. *J. Am. Chem. Soc.* **1976**, *98*, 4679–4681.
(15) For examples of previous conjugate addition reactions and enolate anion alkylation, see: (a) Stork, G. *Pure Appl. Chem.* **1975**, *43*, 553–585; **1968**, *17*, 383–401; (b) Posner, G. H.; Sterling, J. J.; Whitten, C. E.; Lentz, C. M.; Brunelle, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 107–118; (c) Posner, G. H.; Whitten, C. E.; Sterling, J. J.; Brunelle, D. J. *Tetrahedron Lett.* **1974**, 2591–2594; (d) Posner, G. H. *Org. React.* **1972**, *19*, 1–113.
(16) (a) Julia, M.; Blasioli, C. *Bull. Soc. Chim. Fr.*, **1976**, 1941–1946; (b) Stacy, G. W.; Mikulec, R. A., "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. 4, pp 13–15.
(17) Borden, W. T.; Ravindranathan, T. *J. Org. Chem.* **1971**, *36*, 4125–4127.
(18) Lansbury, P. T.; Wang, N. Y.; Rhodes, J. E. *Tetrahedron Lett.* **1971**, 1829–1832. Lansbury, P. T.; Nazarenko, N. *Ibid.* **1971**, 1833–1836. Stork, G.; Clarke, F. H., Jr. *J. Am. Chem. Soc.* **1961**, *83*, 3114–3125. Barrett, J. W.; Linstead, R. P. *J. Chem. Soc.* **1935**, 436–442.
(19) For a similar alkylation in a 2-methylbicyclo[3.3.0]octan-3-one system, see: Nozoe, S.; Furukawa, J.; Sankawa, U.; Shibata, S. *Tetrahedron Lett.* **1976**, 195–198.
(20) The same degree of stereoselectivity in the alkylation of the enolate anion of ketone **9** to compound **10** was observed by Professor R. M. Coates and co-workers, University of Illinois. We wish to thank Professor Coates for information regarding his synthesis of (±)-gymnomitrol. See ref 6a.
(21) Hinckley, C. C. *J. Am. Chem. Soc.* **1969**, *91*, 5160–5162. Demarco, P. V.; Elzey, J. K.; Lewis, R. B.; Wenkert, E. *Ibid.* **1970**, *92*, 5734–5737. The diastereomeric ketone related to ketone **10** has been prepared and characterized via europium-induced NMR shifts of the corresponding alcohols by Professor R. M. Coates and co-workers at the University of Illinois. See ref 26.

Scheme IV. Synthesis of Tricyclic Silyl Enol Ether 15A[a]



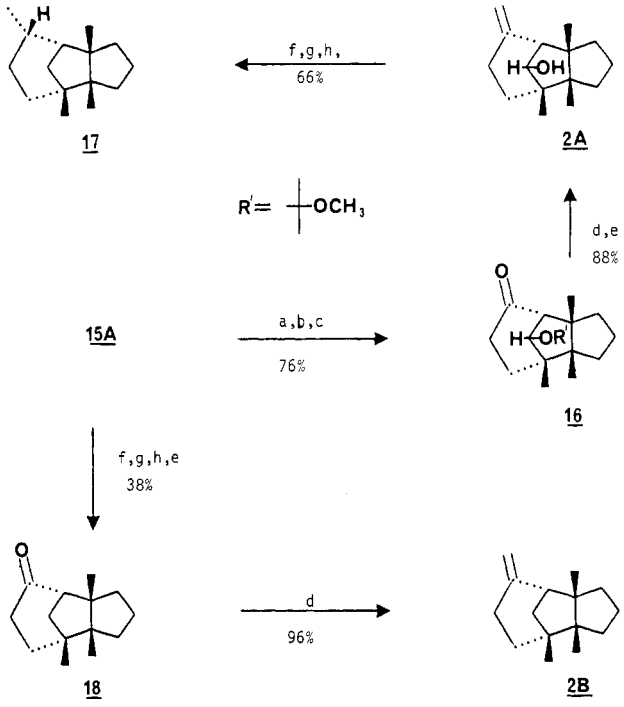
reduction conditions	isomer ratio (15A:15B)	yield, %
i-$Bu_2AlH/C_7H_8/0\ °C/30$ min	6:1	73
$NaBH_4/EtOH/25\ °C/5$ h	16:1	87
$NaBH_4/MeOH/-30\ °C/45$ min	100:0	92

[a] (a) Sia_2BH, THF. (b) H_2O_2, OH^-. (c) H_2CrO_4, acetone. (d) CH_2N_2, Et_2O (small scale) or CH_3I, K_2CO_3, acetone (large scale). (d) $NaN(SiMe_3)_2$, DME. (e) Ac_2O. (e) Ac_2O. (f) $LiN(SiMe_3)_2$, THF. (g) t-$BuMe_2SiCl$, HMPA.

tudes for the europium-induced NMR shifts (Scheme III) for the methyl groups in these two isomers are quite different. In both the major isomer **11A** (β-OH) and the minor isomer **11B** (α-OH) the methyl groups at carbon 1 move at faster rates than the corresponding two bridge methyl groups; however, the relative slopes for the shifts of all six methyl groups in **11A,B** were inversely proportional to the distance of each methyl group from the europium-coordinated hydroxyl substituent as measured with Drieding stereomodels. These data are consistent with the stereochemical assignment of all three methyl groups being on the same face of the bicyclic system and not compatible with the corresponding diastereomers at carbon 1. This analysis is in agreement with a similar analysis of the NMR shifts observed by Coates and co-workers for the two alcohols produced upon reduction of the diastereomer of ketone **10**.[6a,20]

Hydroboration of ketoalkene **10** (Scheme IV) with excess disiamylborane in THF followed by oxidation with basic hydrogen peroxide gives diol **12** in 82% yield.[22] Oxidation of diol **12** with Jones reagent[23] and esterification of the resultant keto acid with ethereal diazomethane affords keto ester **13** in 84% yield. The tricyclic structure of gymnomitrol (**2A**) now requires an intramolecular Claisen condensation on keto ester **13**. The rationale for performing a modified Claisen condensation on keto ester **13** is as follows: (a) differentiation between the two potential carbonyl moieties, (b) selective and stereoselective reduction of the cyclopentanone carbonyl, and (c) ease of protection of the resultant cyclopentanol and unmasking of the protected cyclohexanone. At first the Claisen condensation was performed by using 2-3 equiv of either lithium or sodium bis(trimethylsilyl)amide[24] in a variety of solvents (C_6H_6, DME, or THF) followed by enolate anion trapping with freshly distilled acetic anhydride; however, the yields of these reactions were usually low and capricious. In one experiment, however, tricyclic keto enol

Scheme V. Syntheses of (±)-Gymnomitrol (2A) and (±)-Gymnomitrene (2B)[a]



[a] (a) $CH_2=C(OMe)CH_3$, $POCl_3$ (catalyst), CH_2Cl. (b) n-Bu_4NF, THF. (c) Chromatography on silica gel using 20% Et_2O–80% petroleum ether as an eluant. (d) $Ph_3P=CH_2$, Me_2SO. (e) 5% HCl, CH_3OH. (f) LDA, THF. (g) $ClPO(NMe_2)_2$. (h) Li, $EtNH_2$, Et_2O, t-BuOH.

acetate **14A** was isolated in 63% yield after treatment of keto ester **13** with 2.5 equiv of sodium bis(trimethylsilyl)amide in refluxing DME followed by quenching with acetic anhydride. In subsequent experiments the modified intramolecular Claisen condensation was worked up by a sequential addition of HMPA and *tert*-butyldimethylsilyl chloride to give tricyclic silyl enol ether **14B** reproducibly in good yields. Addition of keto ester **13** to a solution of 2.1 equiv of lithium bis(trimethylsilyl)amide[24] in anhydrous THF/hexane (95:5 ratio, respectively) at reflux over a period of 1 h followed by continued heating at reflux for an additional 140 min, cooling to 0 °C, introduction of HMPA, and enolate anion trapping with *tert*-butyldimethylsilyl chloride[25,26] affords tricyclic ketone **14B** in 65% yield. Stereoselective reduction of ketone **14B** with sodium borohydride in absolute methanol at −30 °C for 45 min gives alcohol **15A** in 92% yield.[25,27] Other reducing agents, solvents, and conditions (Scheme IV) were found to be less stereoselective.

Sequential treatment of silyl enol ether alcohol **15A** (Scheme V) with 2-methoxypropene in dichloromethane in the presence of a catalytic amount of phosphorus oxychloride[28] at room temperature for 16 h followed by the addition of a solution of tetra-*n*-butylammonium fluoride[25] in THF and continued stirring at room temperature for 10 h produces keto ketal **16** [R = $C(CH_3)_2OCH_3$] in 74% overall yield after chromatography on silica gel. Thus, sequential protection and desilylation in a one-pot reaction is both a convenient and efficient process. Finally, a Wittig

(22) Zweifel, G.; Brown, H. C. *Org. React.* **1963**, *13*, 1–54.
(23) Bowden, K.; Heilbron, J. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39–45. Djerassi, C.; Engle, R. R.; Bowers, A. *J. Org. Chem.* **1956**, *21*, 1547–1549.
(24) Wannagat, U.; Nierderprüm, H. *Chem. Ber.* **1961**, *94*, 1540–1547. Amonoo-Neizer, E. H.; Shaw, R. A.; Skovlin, D. O.; Smith, B. C. *J. Chem. Soc.* **1965**, 2997–2999.
(25) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191.
(26) Clark, R. D.; Heathcock, C. H. *J. Org. Chem.* **1976**, *41*, 1396–1403.
(27) The diastereomeric alcohol is more conveniently separated by chromatography on silica gel after the formation of the methoxyacetone ketal **16**.
(28) Kluge, A. F.; Untch, K. G.; Fried, J. H. *J. Am. Chem. Soc.* **1972**, *94*, 7827–7832.

reaction of keto ketal **16** with methylenetriphenylphosphorane[29] in anhydrous dimethyl sulfoxide at 75 °C for 16 h and subsequent methanolysis in the presence of a catalytic amount of 5% HCl solution at room temperature for 0.5 h afford (±)-gymnomitrol (**2A**) in 88% yield (~7% overall yield from ketone **3**). Synthetic gymnomitrol (**2A**) was observed to be identical with a sample of the natural substance with respect to GLC, TLC, and IR, NMR, and mass spectral data.

In an effort to convert synthetic gymnomitrol (**2A**) to (±)-gymnomitrene (**2B**), we treated alcohol **2A** with lithium diisopropylamide in THF followed by *N,N,N',N'*-tetramethylphosphorodiamidic chloride (TPDC) to give an intermediate phosphate ester in 69% yield. Attempted reduction of this phosphate ester with lithium metal in liquid ammonia at −33 °C in the presence of *tert*-butyl alcohol gave only returned starting phosphate ester unaffected. However, reduction of this intermediate phosphate ester under the conditions of Ireland and co-workers[30] with 10 equiv of lithium metal in ethylamine–ether in the presence of *tert*-butyl alcohol at 0 °C gave (±)-dihydrogymnomitrene (**17**) in 66% overall yield from (±)-gymnomitrol (**2A**). The secondary methyl substituent in hydrocarbon **17** is assumed to be equatorially situated. Examination of the Dreiding stereomodel for the intermediate radical anion involved in the reduction of the exocyclic alkene suggests that the kinetically controlled protonation or hydrogen atom transfer should occur from the stereochemically less hindered β face of the molecule to afford an equatorially oriented secondary methyl group. The failure of this approach to prepare (±)-gymnomitrene (**2B**) resulted in a reevaluation of *tert*-butyldimethylsilyl enol ether **15A** as a potential synthetic intermediate to sesquiterpene **2B**. Sequential treatment of compound **15A** with lithium diisopropylamide in THF followed by TPDC gives the corresponding phosphate ester in 62% yield. Reduction of this intermediate phosphate ester under the conditions of Ireland and co-workers[30] at −4 °C followed by hydrolysis of the silyl enol ether functionality affords tricyclic ketone **18** in 38% overall yield from alcohol **15A**. Thus the modified Claisen condensation product **14B** serves a dual purpose in the synthesis of both naturally occurring substances **2A,B**. Finally, a Wittig reaction of ketone **18** with methylenetriphenylphosphorane in dimethyl sulfoxide at 75 ± 2 °C for 20 h produces (±)-gymnomitrene (**2B**) in 96% yield. The IR, NMR, and mass spectral data for synthetic hydrocarbon **2B** were identical with those reported for the naturally occurring sesquiterpene.

Experimental Section

Materials and Techniques. Melting points were determined on Büchi capillary melting point apparatus. All melting points and boiling points are uncorrected and are reported in degrees Celsius. Evaporative distillation refers to bulb-to-bulb short-path distillation in which the bulb was heated in an Aldrich Kugelrohr apparatus (catalog No. Z10,046-3). The temperature cited for these distillations refers to the temperature attained by the air chamber during the distillation. Microanalyses were performed by Spang Microanalytical Laboratory. Analytical gas-phase chromatography (GLC) was performed on a Varian Aerograph Model 1400 equipped with a flame-ionization detector with helium as the carrier gas and using the following types of columns and flow rates: (a) 5-ft, stainless-steel, $^1/_8$-in. column packed with 3% SE-30 on Varaport-30 (100/120 mesh, Varian), flow rate 15 mL/min at ambient temperature; (b) 6-ft, stainless-steel, $^1/_8$-in. column packed with 5% OV-17 on Varaport-30 (80/100 mesh, Varian), flow rate 15 mL/min at ambient temperature. Silica gel PF 254 + 366 (E. Merck No. 7748) and silica gel 60 (E. Merck No. 7734, 70–230 or 75–325 mesh) available from Brinkmann Instruments were used for thin-layer and column chromatography, respectively. Liquid chromatography was performed on (a) a Waters Associates high-pressure liquid chromatograph, Model 201, equipped with a Model M-6000 pump, or (b) a medium-pressure liquid chromatograph consisting of a Fluid laboratory pump, Model RPSYX, and Brinkmann prepacked columns A, B, and C having column volumes of 16, 130, and 430 mL, respectively, or columns packed with silica gel 60 (E. Merck No. 9385, 230–400 mesh, available from Brinkmann Instruments).[31] Infrared (IR) spectra were recorded on a Perkin-Elmer Model 237B. Samples were taken in spectroquality CCl_4 or $CHCl_3$ by using balanced 0.1-mm NaCl solution cells or were taken as thin films between NaCl plates. Nuclear magnetic resonance (NMR) spectra were measured on Varian Associates Model T-60 and Model XL-100 spectrometers in the solvents indicated. High-resolution mass spectra were obtained on a Du Pont Flash CEC 21-110 B spectrometer at 70 eV. Low-resolution mass spectra were recorded on a Finnigan 3300 spectrometer at 25 eV.

Ether (Et_2O), tetrahydrofuran (THF), and 1,2-dimethoxyethane (DME) were purified by fresh distillation of anhydrous commercial solvents from $LiAlH_4$ under N_2 immediately before use in all reactions. Pentane and CH_2Cl_2 were distilled from P_2O_5. Diisopropylamine, bis(trimethylsilyl)amine, and *tert*-butyl alcohol were distilled from CaH_2 (−40 mesh) under N_2. Hexamethylphosphoric triamide (HMPA) was vacuum distilled from CaH_2 (−40 mesh) onto freshly activated type 13X molecular sieves. Dimethyl sulfoxide was vacuum distilled (3×) from 95% CaH_2 (−40 mesh)–5% $NaNH_2$, with the last distillation onto freshly activated type 4A molecular sieves. Finally for all reactions performed under an atmosphere of dry N_2, the equipment was dried in an oven at 120 °C for several hours and then allowed to cool in an atmosphere of dry N_2 by using an apparatus designed by Johnson and Schneider.[32] All liquid transfers were made with nitrogen-filled syringes. The term "petroleum ether" refers to the Baker "analyzed reagent", bp 30–60 °C. The usual workup procedure consisted of extraction of the organic product from an ice-cold aqueous layer with Et_2O (3–6×). The combined ethereal extracts were then washed with saturated NaCl solution (1×), dried over anhydrous $MgSO_4$ (powder) or Na_2SO_4 (granular), filtered through anhydrous $MgSO_4$, and concentrated in vacuo. The nomenclature utilized is that preferred by Chemical Abstracts.[33]

2-Methyl-2-(2-bromo-2-propenyl)cyclopentanone (4B).[7,11] A small amount of 2,2'-bipyridine (0.01 g, Aldrich) was placed in a 500-mL, three-necked, round-bottomed flask equipped with a magnetic stirring bar and a pressure-equalizing dropping funnel under a N_2 atmosphere. The reaction flask was then cooled to −40 ± 2 °C (dry ice/acetone bath), and anhydrous THF (80 mL) and MeLi (2.06 M in Et_2O, 45.2 mL, 0.093 mol) were added, followed by dropwise addition of diisopropylamine (13.2 mL, 0.94 mol) over a period of 30 min. After the mixture was stirred at this temperature for 45 min, 2-methylcyclopentanone (9.23 g, 0.094 mol) was added through the dropping funnel in a dropwise manner over a period of 30 min. After the mixture was stirred for 1 h, the dry ice/acetone bath was removed, and the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h, the reaction mixture was cooled to 0 °C (ice bath), and 2,3-dibromopropene (10.7 mL, 0.104 mol, freshly distilled) was added rapidly via syringe. After the mixture was stirred at 0 °C for 1 h, the ice bath was removed, and the reaction mixture was allowed to warm to room temperature and then stirred overnight (15 h). The resulting yellow solution was poured into an ice–NH_4Cl solution and worked up in the usual way with an initial $Na_2S_2O_3$ wash to afford 20.4 g of yellow oil. Chromatography on

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silica gel (500 g) in a 2.0-cm-diameter column, using a solution of 10% Et_2O–90% petroleum ether (v/v) with 10 drops of pyridine in 1 L of solution to elute 150-mL fractions, gave 16.2 g (79%) of pure ketone **4B** in fractions 17–25. Evaporative distillation gave colorless liquid ketone **4B**: bp 40–43 °C (1.9 mmHg); IR (CCl_4) 2964 (CH, aliphatic), 1740 (C=O), 1625 cm^{-1} (C=C); NMR (CCl_4) δ 5.54 (m, 2, CH_2=), 2.61 (s, 2, CH_2BrC=), 1.00 (s, 3, CH_3); GLC column a (column temperature 100 °C) retention time 13.5 min, column b (column temperature 150 °C) retention time 8.25 min. Anal. Calcd for $C_9H_{13}OBr$: C, 49.79; H, 6.04; Br, 36.80. Found: C, 50.02; H, 6.12; Br, 36.66.

2-Methyl-2-(2-propynyl)cyclopentanone (4C).[7,11] A small amount of 2,2′-bipyridine was placed in a 250-mL, three-necked, round-bottomed flask equipped with a press-equalizing dropping funnel and a magnetic stirring bar. Anhydrous DME (80 mL) was added, and the reaction flask was cooled to −50 °C (dry ice/acetone bath). *n*-Butyllithium (1.6 M solution in hexane, 60.4 mL, 0.097 mol, Aldrich) was added, followed by the dropwise addition of diisopropylamine (13.5 mL, 0.097 mol) over a period of 30 min. After the mixture was stirred for 1 h, ketone **3** (10 g, 0.098 mol) was added through the dropping funnel over a period of 30 min. After this mixture was stirred for 1.5 h, the dry ice/acetone bath was removed, and the reaction mixture was allowed to warm to room temperature. After being stirred for 4 h, the reaction mixture was then cooled to 0 °C, and propargyl bromide (11.5 mL of an 80% solution in toluene, 0.22 mol, freshly distilled, Aldrich) was added rapidly. After being stirred for 1 h, the reaction mixture was then allowed to warm to room temperature and stirred overnight (14 h). The resulting yellow solution was poured into an ice–NH_4Cl solution and extracted with Et_2O (6 × 40 mL). The combined ethereal extracts were washed with $Na_2S_2O_3$ solution (3 × 30 mL) and then worked up in the usual way to afford 14.1 g of a yellow liquid. Medium-pressure LC on silica gel 60, using a solution of 10% ether–90% petroleum ether (v/v), gave 10.6 g (73%) of pure ketone **4C**. Evaporative distillation [bp 30–33 °C (2.8 mmHg)] of a small sample gave pure **4C** as a colorless liquid: IR (CCl_4) 3320 (CH, alkyne), 2964 (CH, aliphatic), 2138 (C≡C, monosubstituted alkyne), 1744 cm^{-1} (C=O); NMR (CCl_4) δ 2.24 (s, 2, $CH_2C{\equiv}C$), 2.19 (s, 1, C≡CH), 1.06 (s, 3, CH_3); GLC column a (column temperature 100 °C) retention time 2.6 min. Anal. Calcd for $C_9H_{12}O$: C, 79.49; H, 8.88. Found: C, 79.10; H, 8.65.

2-Methyl-2-(2-oxopropyl)cyclopentanone (7). Method A.[18] Sulfuric acid (90%, 40 mL) was placed in a 25-mL, round-bottomed flask and cooled to 0 °C (ice bath), and ketone **4B** (0.783 g, 0.0036 mol) was added dropwise over a period of 40 min. After the mixture was stirred for 1 h, the ice bath was removed and the reaction mixture allowed to stir at room temperature for 20 h. The resulting light brown solution was then poured onto ice and worked up in the usual way to afford 0.811 g of yellow oil. Chromatography on silica gel (80 g), using a solution of 30% ether–70% petroleum ether (v/v) to elute the column, gave 0.506 g (91%) of pure diketone **7**.

Method B.[11a] Mercury(II) acetate (10.39 g, 0.033 mol, J. T. Baker) was placed in a 250-mL, three-necked, round-bottomed flask. Formic acid (88%, 157 mL, Fisher Scientific) was then added. After all the $Hg(OAc)_2$ had completely dissolved, a solution of ketone **4B** (7.078 g, 0.033 mol) in CH_2Cl_2 was added dropwise via a pressure-equalizing dropping funnel over a period of 40 min. After the mixture was stirred at room temperature for 24 h, the resulting clear solution with a white precipitate was poured into an ice–NaCl solution, and the flask was rinsed with saturated NaCl solution. The aqueous layer was separated and extracted with Et_2O (7 × 50 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution until the solution was neutral (7 × 50 mL), water (7 × 50 mL), and saturated NaCl (2 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo to afford 4.89 g of yellow oil. Medium-pressure chromatography, using prepacked column C and a solution of 40% ether–60% petroleum ether (v/v) to elute the column, gave 4.58 g (91%) of pure **7**.

Method C.[11b] Mercury(II) oxide (0.757 g, 3.49 mmol, J. T. Baker) was placed in a 100-mL, three-necked, round-bottomed flask equipped with a pressure-equalizing dropping funnel and a magnetic stirring bar. Concentrated H_2SO_4 (3 mL) and H_2O (32 mL) were then added. The reaction was heated to 60 °C (external temperature, oil bath), and ketoalkyne **4C** (8.28 g, 0.068 mol) dissolved in CH_2Cl_2 (3 mL) was added through the dropping funnel over a period of 45 min. After the addition was completed, the reaction mixture was then heated for an additional 10 min. The resulting cloudy white suspension was then worked up in the usual way to afford 8.48 g of crude yellow liquid. Medium-pressure liquid chromatography on prepacked column C, using a solution of 40% ether–60% petroleum ether (v/v) to elute the column, gave 7.53 g (80%) of diketone.[7] Evaporative distillation gives a pure colorless liquid, **7**: bp 31–34 °C (2.2 mmHg); IR (CCl_4) 2953 (CH, aliphatic), 1737 (C=O), 1720 cm^{-1} (C=O); NMR (CCl_4) δ 2.64 (d, 2, J = 3 Hz, $COCH_2$), 2.05 (s, 3, CH_3CO), 0.93 (s, 3, CH_3); GLC column a (column temperature 100 °C) retention time 7.9 min, column b (column temperature 150 °C) retention time 5.5 min. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.51; H, 9.50.

4,5,6,6a-Tetrahydro-6a-methyl-2(1*H*)-pentalenone (8).[14] **Method A.** Potassium hydroxide (assay 86%, 7.33 g, 0.111 mol) and 95% EtOH (400 mL) were placed in a 1-L, round-bottomed flask equipped with a magnetic stirring bar, a dropping funnel, and a reflux condenser. The solution was heated to reflux under N_2. Diketone **7** (7.44 g, 0.482 mol) in 95% EtOH (75 mL) was added through the dropping funnel over a period of 1.5 h. After an additional 2 h at reflux, the reaction mixture was then allowed to cool to room temperature and worked up in the usual way to give 6.80 g of crude product. Chromatography on silica gel (60 g) using 40% ether–60% petroleum ether (v/v) to elute the column gave 5.71 g (84%) of pure enone **8** as a colorless liquid.

Method B. Potassium *tert*-butoxide (98%, 1.507 g, 0.013 mol) and anhydrous *t*-BuOH (120 mL) were placed in a 500-mL, round-bottomed flask under N_2. Diketone **7** (1.787 g, 0.0116 mol) in anhydrous *t*-BuOH (10 mL) was added through the dropping funnel over a period of 45 min at room temperature. After being stirred for 1 h 10 min at room temperature, the reaction mixture was then poured into an ice–NH_4Cl solution and worked up in the usual way to give 1.64 g of crude product. Column chromatography on silica gel, using a solution of 40% ether–60% petroleum ether (v/v) to elute the column, gave 1.22 g (77%) of pure enone **8**. Evaporative distillation [bp 25–27 °C (3.4 mmHg)] gave colorless liquid **8** for analysis: IR (CCl_4) 2964 (CH, aliphatic), 1715 (C=O), 1627 cm^{-1} (C=C); NMR (CCl_4) δ 5.71 (m, 1, COCH=), 2.23 (s, 2, $COCH_2$), 1.15 (s, 3, CH_3); GLC column a (column temperature 120 °C) retention time 3.9 min, column b (column temperature 150 °C) retention time 3.3 min. Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.43; H, 8.78.

(3aα,6aα)-Hexahydro-3a,6a-dimethyl-2(1*H*)-pentalenone (6).[6a,c,17] Copper(I) iodide (0.0924 g, 0.485 mmol) was placed in a 25-mL, round-bottomed flask under N_2. The flask was cooled to −78 °C (dry ice/acetone bath), and anhydrous Et_2O (1.0 mL) was added, followed by addition of MeLi (2.06 M in Et_2O, 0.47 mL, 0.98 mmol) slowly over a period of 5 min. The resulting clear solution was allowed to stir at −78 °C for 45 min, and then a solution of enone **8** (0.0551 g, 0.402 mmol) in Et_2O (2.5 mL) was added dropwise. The cooling bath was removed, after warming to room temperature over a period of 1 h, the reaction mixture was quenched with saturated NH_4Cl solution (10 mL), and the resulting solution was worked up in the usual way to give 0.0597 g of crude product. Chromatography on prepacked column C, using a solution of 10% Et_2O–90% petroleum ether (v/v) to elute the column, gave 0.0527 g (86%) of pure ketone **6**: mp 48–49 °C; IR (CCl_4) 2953 (CH, aliphatic), 1742 cm^{-1} (C=O); NMR (CCl_4) 2.10 (d, 4, J = 2 Hz, CH_2COCH_2), 1.74 (s, 6, $-(CH_2)_3-$), 1.06 (s, 6, 2 CH_3); GLC column a (column temperature 100 °C) retention time 7.3 min, column b (column temperature 150 °C) retention time 4.12 min. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.95; H, 10.63.

(3aα,6aα)-Hexahydro-3a,6a-dimethyl-1-(2-propenyl)-2-(1*H*)-pentalenone (9).[15] Copper(I) iodide (7.57 g, 0.0398 mol) was placed in a 500-mL, round-bottomed flask under N_2. The flask was then cooled to −78 °C (dry ice/acetone bath), and anhydrous THF (150 mL) was added, followed by addition of MeLi (1.1 M in Et_2O, 72.3 mL, 0.0795 mol) slowly over a period of 20 min. The resulting clear solution was allowed to stir for 1 h, and then enone **8** (4.92 g, 0.0362 mol) dissolved in anhydrous THF (40 mL) was added over a period of 30 min. After the mixture was stirred for 1 h, the dry ice/acetone bath was removed, and the reaction mixture was allowed to warm to room temper-

ature. Anhydrous HMPA (60 mL) was added, followed by allyl chloride (14.7 mL, 0.181 mol, freshly distilled from CaH_2). After being stirred at room temperature overnight (14 h), the reaction mixture was poured into a saturated NH_4Cl solution (300 mL) and extracted with Et_2O (5 × 60 mL). The combined ethereal extracts were washed with $Na_2S_2O_3$ solution (2 × 60 mL), water (10 × 60 mL), and saturated NaCl solution (2 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo to give 7.16 g of yellow liquid. Medium-pressure LC on prepacked column C, using a solution of 10% ether–90% petroleum ether (v/v) to elute the column, gave 5.17 g (74%) of an isomeric mixture of ketones **9** along with 0.512 g (9%) of ketone **6**. Evaporative distillation of the mixture of ketones **9** [bp 55–58 °C (2.8 mmHg)] gave a colorless liquid: IR (CCl_4) 3084 (CH, alkene), 2953 (CH, aliphatic), 1737 (C=O), 1638, 995, 915 cm^{-1} (C=C); NMR (100 MHz, $CDCl_3$) δ 4.86–6.14 (m, 3, $CH{=}CH_2$), 2.11 (s, 2, $COCH_2$), 1.06 (s, 0.6 CH_3), 1.05 (s, 0.6 CH_3), 1.02 (s, 0.4 CH_3), 0.86 (s, 0.4 CH_3); the NMR ratio of ketones **9** was ~60:40; GLC column a (column temperature 140 °C) retention time 4.9 min (one peak), column b (column temperature 170 °C) retention time 5.5 min. Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.13; H, 10.54.

Alkylation of 1,5-Dimethylbicyclo[3.3.0]octan-3-one (6).[7,11] A small amount of 2,2′-bipyridine and anhydrous THF (25 mL) were placed in a 100-mL, round-bottomed flask under N_2. The reaction was cooled to −50 °C (dry ice/acetone bath), and *n*-BuLi (1.6 M in hexane, 9.8 mL, 0.0157 mol, Aldrich) was added, followed by diisopropylamine (2.2 mL, 0.0157 mol). After the mixture was stirred for 1 h, ketone **6** (2.52 g, 0.0165 mol) dissolved in anhydrous THF (30 mL) was added over a period of 30 min. After this mixture was stirred for 1 h, the dry ice/acetone bath was removed, and the reaction mixture was allowed to warm to room temperature. After the mixture had been stirred for 3 h, anhydrous HMPA (7.5 mL) was added, followed by allyl bromide (2.86 mL, 0.033 mol, freshly distilled from CaH_2), and the reaction mixture was then allowed to stir at room temperature overnight. The reaction mixture was poured into an ice–NH_4Cl solution and extracted with Et_2O (5 × 30 mL). The combined ethereal extracts were washed with 10% $Na_2S_2O_3$ solution, (25 mL), NaCl solution (2 × 30 mL), water (10 × 30 mL), and saturated NaCl solution (2 × 30 mL), dried ($MgSO_4$), and concentrated in vacuo to give 3.35 g of yellow liquid. Medium-pressure LC on prepacked column C, using a solution of 10% ether–90% petroleum ether (v/v) to elute 50-mL fractions, gave (fractions 30–36) 2.13 g (67%) of a mixture of ketones **9**. The IR and NMR spectra were identical with those obtained from the previous reaction.

(1α,3aβ,6aβ)-Hexahydro-1,3a,6a-trimethyl-1-(2-propenyl)-2(1*H*)-pentalenone (10).[7,11,19] Sodium hydride (0.311 g, 7.91 mmol, 61.14% dispersion in oil, Ventron) was placed in a 100-mL, round-bottomed flask and was washed with anhydrous Et_2O (3 × 20 mL), and the remaining Et_2O was removed under high vacuum. Anhydrous DME was added under N_2, followed by a mixture of ketones **9** (1.38 g, 719 mmol) in anhydrous DME (4.0 mL). The reaction mixture was stirred at room temperature for 4 h, cooled to 0 °C (ice bath), and charged with CH_3I (0.89 mL, 14.4 mmol). After the mixture was stirred at 0 °C for 1 h, the ice bath was removed, and the reaction mixture was allowed to stir at room temperature overnight (15 h). The resulting yellow solution was poured into ice–water (50 mL) and extracted with Et_2O (5 × 20 mL). The combined ethereal extracts were washed with 10% $Na_2S_2O_3$ solution (2 × 20 mL), H_2O (4 × 20 mL), and saturated NaCl solution (2 × 25 mL), dried ($MgSO_4$), and concentrated in vacuo to give 1.57 g of crude product. Column chromatography on silica gel (140 g), using a solution of 10% ether–90% petroleum ether (v/v) to elute the column, gave 0.954 g (64%) of pure ketone **10**. Evaporative distillation [bp 58–61 °C (2.8 mmHg)] gave colorless liquid ketone **10**: IR (CCl_4) 3074 (CH, alkene), 2953 (CH, aliphatic), 1740 (C=O), 1638, 1000, 920 cm^{-1} (C=C); NMR (100 MHz, $CDCl_3$) δ 4.82–6.60 (m, 3, $CH{=}CH_2$), 2.28 (d, 2, $COCH_2$, J = 4.4 Hz), 1.17 (s, 3, CH_3), 1.05 (s, 3, CH_3), 0.97 (s, 3, CH_3); GLC column a (column temperature 140 °C) retention time 3.9 min, column b (column temperature 170 °C) retention time 9.25 min. Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.65; H, 10.84.

Reduction of (1α,3aβ,6aβ)-Hexahydro-1,3a,6a-trimethyl-1-(2-propenyl)-2(1*H*)-pentalenone (10). Sodium borohydride (0.318 g, 8.40 mmol) was placed in a 25-mL, round-bottomed flask, and 100% EtOH (9 mL) was added under N_2. After the $NaBH_4$ had completely dissolved, the solution was cooled to 0 °C, and ketone **10** (0.215 g, 1.04 mmol) in 100% EtOH (1 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature, stirred for 3 h, quenched with glacial HOAc (3 mL) at 0 °C, and extracted with Et_2O (3 × 15 mL). The combined ethereal extracts were washed with saturated $NaHCO_3$ solution (2 × 10 mL) and saturated NaCl solution (4 × 15 mL), dried (Na_2SO_4), and concentrated in vacuo to give 0.392 g of crude product. Column chromatography on silica gel (4 g, column volume 10 mL), using a solution of 15% ether–85% petroleum ether (v/v) to elute 2-mL fractions, gave 0.044 g (21%) of alcohol **11B** (fractions 7–12) and 0.169 g (78%) of alcohol **11A** (fractions 11–17). Alcohol **11B**: IR (CCl_4) 3693–3156 (OH), 3074 (CH, alkene), 2942 (CH, aliphatic), 1633, 910 cm^{-1} (C=C); NMR (CCl_4) δ 4.8–6.3 (m, 3, $CH{=}CH_2$), 3.83 (m, 1, CHOH), 1.08 (s, 3, CH_3), 0.83 (s, 3, CH_3), 0.80 (s, 3, CH_3). Alcohol **11A**: IR (CCl_4) 3694–3157 (OH), 3074 (CH, alkene), 2942 (CH, aliphatic), 1633, 910 cm^{-1} (C=C); NMR (CCl_4) δ 4.83–6.43 (m, 3, $CHCH_2$), 4.17–3.87 (m, 1, CHOH), 1.02 (s, 3, CH_3), 0.85 (s, 6, 2 CH_3); GLC for alcohol **11B** column a (column temperature 140 °C) retention time 2.9 min, column b (column temperature 170 °C) retention time 11.9 min; GLC for alcohol **11A** column a (column temperature 140 °C) retention time 4.9 min, column b (column temperature 170 °C) retention time 12.6 min. These two alcohols were utilized for the europium-induced NMR shift analysis (Scheme III) without further purification. Anal. Calcd for $C_{14}H_{24}O$ (**11A,B**): C, 80.71; H, 11.61. Found: C, 80.60; H, 11.66.

Octahydro-2-hydroxy-1,3a,6a-trimethyl-1-pentalenepropanol (12).[22] 2-Methyl-2-butene (1.02 mL, 9.59 mmol, freshly distilled from Na metal) was added into a 50-mL, round-bottomed flask, followed by anhydrous THF (12 mL) under N_2. The reaction was cooled to 0 °C (ice bath), BH_3·THF (1 M in THF, 4.8 mL, 4.79 mmol, Ventron) was added slowly, the ice bath was then removed, and the reaction was allowed to stir at room temperature for 3 h. The resulting solution was cooled to 0 °C, and ketone **10** (0.20 g, 0.959 mmol) in anhydrous THF (3 mL) was added over a period of 30 min. After being stirred at room temperature overnight, the reaction mixture was cooled to 0 °C and carefully quenched with H_2O (1 mL) immediately followed by a 30% H_2O_2–10% NaOH solution (2.5 mL each). After the mixture was stirred at 0 °C for 3 h, the ice bath was removed, and the reaction mixture was allowed to stir at room temperature for 3 h. The reaction mixture was then poured into H_2O (90 mL) and extracted with Et_2O (5 × 20 mL). The combined ethereal extracts were washed with 10% NaOH solution (20 mL), H_2O (2 × 20 mL), and saturated NaCl solution (2 × 20 mL), dried (Na_2SO_4), and concentrated in vacuo. After excess 3-methyl-2-butanol had been removed under high vacuum, 0.226 g of crude product was obtained. Column chromatography on silica gel (25 g), using a solution of 50% ether–50% petroleum ether (v/v) to develop the column, gave 0.178 g (82%) of pure diol **12** as a white crystalline solid. Recrystallization of a small sample from $CHCl_3$/petroleum ether gave analytically pure diol **12**: mp 131–132 °C; IR ($CHCl_3$) 3621, 3430 (OH), 2942 (CH, aliphatic), 1110 cm^{-1} (CO); NMR ($CDCl_3$, acetone-d_6) δ 4.3–3.2 (m, 3, CH_2OH), 2.55 (s, 2, 2 OH), 1.01 (s, 3, CH_3), 0.86 (s, 3, CH_3), 0.84 (s, 3, CH_3). Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. Found: C, 74.02; H, 11.50.

Methyl (1α,3aβ,6aβ)-Octahydro-1,3a,6a-trimethyl-2-oxo-1-pentalenepropanoate (13). A solution of diol **12** (1.01 g, 4.46 mmol) in reagent grade acetone (15 mL) was placed in a 50-mL, round-bottomed flask. The reaction was cooled to 0 °C (ice bath), and Jones reagent[19] (18 mL, 2.67 M, 4.81 mmol) was added dropwise over a period of 30 min. After the mixture was stirred for 30 min, the excess oxidizing reagent was quenched with reagent grade *i*-PrOH until the orange color disappeared in the upper layer of the two-phase mixture. The reaction mixture then was diluted with H_2O (150 mL) and extracted with Et_2O (4 × 50 mL). The combined ethereal extracts were washed with 10% NaOH solution (4 × 30 mL). The combined aqueous layers were cooled with an ice bath, acidified with concentrated HCl, and then extracted with Et_2O (5 × 50 mL). The combined ethereal extracts were washed with H_2O (4 × 40 mL) and saturated NaCl solution (2 × 40 mL), dried (Na_2SO_4), and concentrated in vacuo to afford 1.16 g of crystalline keto acid. Recrystallization of the crude product from Et_2O/petroleum ether afforded 0.963 g (91%) of keto acid: mp

65–66 °C; IR (CCl_4) 2953 (CH, aliphatic), 1731 (C=O, aliphatic), 1709 cm^{-1} (C=O, CO_2H); NMR (CCl_4) δ 10.86 (s, 1, CO_2H), 2.20 (s, 2, $COCH_2$), 1.18 (s, 3, CH_3), 1.03 (s, 3, CH_3), 0.96 (s, 3, CH_3). Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.80; H, 9.38.

Method A. An excess of ethereal diazomethane was added dropwise to a solution of the above keto acid in Et_2O at 0 °C (ice bath). The solution was maintained at 0 °C for 30 min, and then the excess diazomethane was quenched with methanol. The solution was then concentrated in vacuo to give 0.715 g of yellow liquid. Column chromatography on silica gel, using a solution of 40% Et_2O–60% petroleum ether (v/v) to develop the column, afforded 0.675 g (92%) of pure keto ester **13**.

Method B. To a stirred solution of anhydrous K_2CO_3 (1.27 g, 9.20 mmol) in acetone (30 mL) was added a sample of the above keto acid (1.46 g, 6.13 mmol) in acetone (5 mL), followed by CH_3I (1.2 mL, 18.4 mmol). After the mixture was stirred at room temperature for 2 h under N_2, 10% K_2CO_3 solution (20 mL) was added, and the reaction mixture was transferred to a separatory funnel and extracted with Et_2O (5 × 20 mL). The combined ethereal extracts were washed with H_2O (2 × 20 mL) and saturated NaCl solution (2 × 20 mL), dried ($MgSO_4$), and concentrated in vacuo to give 1.49 g of crude product. Column chromatography on silica gel, using a solution of 40% Et_2O–60% petroleum ether (v/v) to elute the column, gave 1.44 g (93%) pure keto ester **13**. Evaporative distillation [bp 65–69 °C (2.8 mmHg)] gave a colorless liquid: IR (CCl_4) 2948 (CH, aliphatic), 1734 cm^{-1} (C=O); NMR (CCl_4) δ 3.62 (s, 3, CO_2CH_3), 2.30 (s, 2, $COCH_2$), 1.16 (s, 3, CH_3), 1.01 (s, 3, CH_3), 0.98 (s, 3, CH_3); GLC column a (column temperature 170 °C) retention time 5.9 min; low-resolution mass spectrum, m/z (relative intensity) 252 (m^+, 12), 221 (7), 196 (28), 95 (100), 55 (40), 41 (66). Anal. Calcd for $C_{15}H_{24}O_3$: m/e 252.1725. Found: m/e 252.1728 (mass spectrum), 1.2-ppm error (by high-resolution mass spectroscopy).

(3aα,4aα,8aα,8aα)-7-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1,2,3,3a,4,5,8,8a-octahydro-3a,4,8a-trimethyl-4,8-methanoazulen-9-one (14B).[24-26] To a stirred solution of *n*-BuLi (2.5 mL, 1.5 M solution in hexane, 3.77 mmol) at −50 °C (dry ice/acetone bath) was added bis(trimethylsilyl)amine (0.79 mL, 3.77 mmol) under N_2. The resulting solution, containing a small amount of white precipitate, was allowed to stir at −50 °C for 1 h. Anhydrous THF (40 mL) was added, and the solution was allowed to warm to room temperature. This solution was heated to reflux (bath temperature 83–85 °C), and keto ester **13** (0.453 g, 1.80 mmol) dissolved in anhydrous THF (5 mL) was then added dropwise through a dropping funnel over a period of 1 h. After 140 min, the reaction mixture was cooled to 0 °C (ice bath), anhydrous HMPA (11 mL) was added, followed by *t*-BuMe_2SiCl (1.08 g, 7.18 mmol) in anhydrous Et_2O (2 mL), and the reaction mixture was allowed to stir and warm to room temperature overnight. The reaction mixture was diluted and extracted with petroleum ether (4 × 25 mL) and then worked up in the usual way to give 1.5 g of crude product. Column chromatography on silica gel, using a solution of 2% Et_2O–98% petroleum ether (v/v) to elute the column, gave 0.393 g (65%) of pure keto silyl enol ether **14B**. Recrystallization from petroleum ether at −78 °C gave analytically pure **14B** as white crystals: mp 46–46.5 °C; IR (CCl_4) 3046 (CH, alkene), 2958 (CH, aliphatic), 1745 (C=O), 1660, 863 (C=C), 1175 cm^{-1} (CO); NMR (100 MHz, $CDCl_3$) δ 4.65 (t, 1, C=CH, J = 3.3 Hz), 0.97 (s, 3, CH_3), 0.92 (s, 3, CH_3), 0.90 (s, 9, $SiCMe_3$), 0.80 (s, 3, CH_3), 0.15 (s, 3, SiMe), 0.13 (s, 3, SiMe); GLC column a (column temperature 200 °C) retention time 7.7 min; low-resolution mass spectrum, m/z (relative intensity) 334 (m^+, 7), 277 (38), 240 (78), 169 (17), 95 (89), 75 (72), 73 (100), 55 (29), 41 (47). Anal. Calcd for $C_{20}H_{34}O_2Si$: C, 71.80; H, 10.24. Found: C, 71.92; H, 10.30. Calcd for $C_{20}H_{34}O_2Si$: m/e 334.2328. Found: m/e 334.2345 (mass spectrum), 5.1-ppm error (by high-resolution mass spectroscopy).

(3aα,4aα,8aα,8aα)-7-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1,2,3,3a,4,5,8,8a-octahydro-3a,4,8a-trimethyl-4,8-methanoazulen-9-ol (15A). Method A.[25] Keto silyl enol ether **14B** (0.086 g, 0.258 mmol) was added into a 25-mL, round-bottomed flask, followed by anhydrous toluene (1 mL, freshly distilled from CaH_2) under N_2. The reaction was cooled to 0 °C (ice bath), and *i*-Bu_2AlH (0.31 g, 0.387 mmol, 1.25 M in hexane, Texas Alkyls) was added slowly. After being stirred at 0 °C for 30 min, the reaction mixture was poured into an ice–NaOH solution, extracted with Et_2O (4 × 10 mL), and worked up in the usual way to give 0.103 g of crude product. Medium-pressure LC on prepacked column A, using a solution of 15% Et_2O–85% petroleum ether (v/v) to elute the column, gave 0.063 g (73%) of diastereomeric alcohols **15A,B**. The ratio of alcohol **15A** to **15B** was 6:1 (measured as keto acetals **16A,B**).

Method B. Sodium borohydride (0.045 g, 1.18 mmol was added to 100% MeOH (1.5 mL) cooled at −30 °C (dry ice/acetone), and the mixture was allowed to stir for 1 h under N_2. Keto silyl enol ether **14B** (0.078 g, 0.232 mmol) dissolved in 100% MeOH (0.5 mL) was added slowly. After being stirred at −30 °C for 45 min, the reaction mixture was quenched with saturated $NaHCO_3$ solution (3 mL) and worked up in the usual way to give 0.0913 g of crude product. Medium-pressure LC on silica gel with prepacked column A, using a solution of 2% Et_2O–98% petroleum ether (v/v) to elute the column, gave 0.072 g (92%) of alcohol **15A** which was free from its diastereomer by GLC analysis. Evaporative distillation [bp 105–107 °C (2.4 mmHg)] gave **15A** as a colorless gum: IR (CCl_4) 3622 (free OH), 2942 (CH, aliphatic), 1666 (C=C), 1255, 1211 and 1192 cm^{-1} (CO); NMR (CCl_4) δ 4.35 (t, 1, CH=COSi, J = 3 Hz), 3.96 (s, 1, CHOH), 1.19 (s, 3, CH_3), 1.02 (s, 3, CH_3), 0.98 (s, 3, CH_3), 0.93 (s, 9, $SiCMe_3$), 0.16 (s, 6, $SiMe_2$); GLC column a (column temperature 210 °C) retention time 7.95 min; low-resolution mass spectrum, m/z (relative intensity) 336 (m^+, 5), 279 (59), 187 (10), 185 (9), 129 (15), 95 (31), 77 (36), 75 (81), 73 (92), 55 (30), 41 (30). Anal. Calcd for $C_{20}H_{36}O_2Si$: m/e 336.2485. Found: m/e 336.2501 (mass spectrum), 4.8-ppm error (by high-resolution mass spectroscopy).

(3aα,4aα,8aα,8aα)-Octahydro-9-(1-methoxy-1-methylethoxy)-3a,8,8a-trimethyl-4,8-methanoazulen-5(1*H*)-one (16, R = $(CH_3)_2C(CH_3O)O$).[28] To a 25-mL, round-bottomed flask were added alcohol **15A** (0.553 g, 1.64 mmol), anhydrous CH_2Cl_2 (3 mL), 2-methoxypropene (3 mL, freshly distilled), and $POCl_3$ in CH_2Cl_2 solution (0.5 mL, 3 μL/10 mL of solution). After the mixture was stirred at room temperature overnight (16 h), *n*-Bu_4NF in anhydrous THF (14 mL, 3.76 mmol) was added, and the solution was allowed to stir for an additional 10 h. Triethylamine (3 drops) was added to the reaction mixture, which was then poured into an ice–$NaHCO_3$ solution and worked up in the usual way to give 0.656 g of crude product. Medium-pressure LC on silica gel with prepacked column B, using a solution of 20% Et_2O–80% petroleum ether (v/v) to elute the column, gave 0.367 g (76%) of pure keto ketal **16** as a white crystalline solid: mp 75–76 °C; IR (CCl_4) 2953 (CH, aliphatic), 1704 (C=O), 1205, 1148, 1082, 1049 cm^{-1} (CO); NMR (CCl_4) δ 3.85 (s, 1, CHO), 3.16 (s, 3, OCH_3), 2.35 (s, 1, COCH), 1.32 (s, 6, $OCMe_2OMe$), 1.25 (s, 3, CH_3), 1.06 (s, 3, CH_3), 1.02 (s, 3, CH_3); low-resolution mass spectrum, m/z (relative intensity) 294 (m^+, 3), 205 (51), 187 (16), 152 (4), 109 (51), 107 (52), 105 (54), 73 (100), 55 (17), 42 (11). Anal. Calcd for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27. Found: C, 73.12; H, 9.96. Calcd for $C_{18}H_{30}O_3$: m/e 294.2195. Found: m/e 294.2204 (mass spectrum), 3.1-ppm error (by high-resolution mass spectroscopy).

1,2,6-Trimethyl-8-methylenetricyclo[5.3.1.0]undecan-11-ol (Gymnomitrol) (2A).[29] Sodium hydride (0.344 g of a 61.14% suspension in oil, 8.77 mmol) was washed with anhydrous Et_2O (3 × 10 mL) under N_2. The remaining Et_2O was removed under high vacuum. Anhydrous Me_2SO (7 mL) was added, and the resulting mixture was heated at 68 ± 2 °C (oil bath temperature) for 45 min. The oil bath was then removed, and the solution was allowed to cool to room temperature. Methyltriphenylphosphonium bromide (3.65 g, 10.23 mmol) was slowly added in small portions. The resulting bright yellow solution was allowed to stir at room temperature for 30 min, keto ketal **16** (0.208 g, 0.705 mmol) dissolved in anhydrous Me_2SO (2 mL) was added dropwise, and the reaction mixture was heated at 75 ± 2 °C (bath temperature) overnight (16 h). The reaction mixture was cooled to 0 °C (ice bath), diluted with saturated NaCl solution (10 mL), and then worked up in the usual way to give the crude product which was then passed through a silica gel column (6 g) with a solution of 50% Et_2O–50% petroleum ether as an eluting solvent. The crude product obtained was then allowed to stir in MeOH (5 mL) containing 3 drops of 5% HCl/MeOH solution for 30 min. The reaction mixture was neutralized by the dropwise addition saturated $NaHCO_3$ solution. The MeOH was removed in vacuo, and the residue was worked up in the usual way to give 0.183 g

of crude product. Liquid chromatography on silica gel with prepacked column A, using a solution of 20% Et_2O–80% petroleum ether (v/v) as the eluting solvent, gave 0.148 g of (±)-gymnomitrol (**2A**) containing a small amount of impurities. The sample was repurified by column chromatography on 15% silver nitrate–silica gel,[34] using a solution of 10% Et_2O–90% petroleum ether (v/v) as an eluting solvent, to afford 0.137 g (88%) of (±)-gymnomitrol (**2B**) as white crystals. Recrystallization of (±)-gymnomitrol (**2B**) from ethanol–water gave a pure white crystalline solid: mp 104–108 °C; IR (CCl_4) 3620 (free OH), 3060 (CH, alkene), 2932 (CH, aliphatic), 1644, 888 (C=C), 1063 cm^{-1} (CO); NMR ($CDCl_3$, 100 MHz) δ 4.66, 4.64 (2 s, 2, CH_2=), 3.71 (s, 1, CHOH), 2.33 (s, 1, HOCCHC=), 1.24 (s, 3, CH_3), 1.09 (s, 3, CH_3), 0.95 (s, 3, CH_3). The spectral data are identical with those for natural gymnomitrol. Synthetic (±)-gymnomitrol (**1**) was found to have identical retention times with natural gymnomitrol on GLC in both separate and coinjected samples with column a (column temperature 160 °C); retention time 7.6 min. Both natural and synthetic gymnomitrol have the same R_f value on analytical thin-layer chromatography: low-resolution mass spectrum, *m/z* (relative intensity) 220 (m^+, 7), 107 (46), 108 (72), 109 (66), 95 (85), 81 (55), 55 (54), 43 (88), 41 (100). Calcd for $C_{15}H_{24}O$: *m/e* 220.1827. Found: *m/e* 220.1826 (mass spectrum), 0.5-ppm error (by high-resolution mass spectroscopy).

Dihydrogymnomitrene (17).[30] To a stirred solution of MeLi (0.454 mL, 0.500 mmol, 1.10 M) in THF (2.0 mL) at −40 °C (dry ice/acetone bath) was added diisopropylamine under N_2. The resulting solution was stirred at −40 °C for 30 min and then cooled to −78 °C (dry ice/acetone bath), and synthetic alcohol **2A** (0.077 g, 0.350 mmol) dissolved in THF (2.0 mL) was added. The solution was allowed to warm to 0 °C (ice bath) with stirring over a period of 45 min, and then $ClPO(NMe_2)_2$ (0.085 g, 0.058 mL, 0.500 mmol) was added. After being stirred at room temperature for 20 h, the reaction mixture was diluted with H_2O (25 mL) and worked up in the usual way to give 0.12 g of crude product. Chromatography on silica gel (30 g), using 1% MeOH–99% Et_2O as an eluant, gave 0.0843 g (69%) of pure phosphate ester: IR (CCl_4) 1645 cm^{-1} (C=CH_2); NMR (CCl_4) δ 0.95, 1.03, 1.20 (3 s, 9, 3 CH_3), 2.55, 2.70 (2 s, 12, 2 NMe_2), 4.20 (d, *J* = 9 Hz, 1, CHOP), 4.63 (br s, 2, C=CH_2). This phosphate ester (0.067 g, 0.190 mmol) dissolved in Et_2O (5.0 mL) and *t*-BuOH (0.056 g) was added to a solution of Li metal (0.013 g, 1.90 mmol) in $EtNH_2$ (25 mL, double-distilled from Li metal) at 0–5 °C (ice bath). After being stirred for 20 min, the reaction mixture was quenched with *t*-BuOH, the $EtNH_2$ was allowed to evaporate, and the residue was taken up in H_2O (25 mL) and worked up in the usual way to give 0.051 g of crude product. Chromatography on silica gel (10 g) using petroleum ether as the eluant gave 0.037 g (95%) of dihydrogymnomitrene (**17**): bp 50–60 °C (0.3 mmHg); mp 52–55 °C; NMR (CCl_4) δ 0.78 (s, 3, CH_3), 0.87 (s, 3, CH_3), 1.00 (s, 3, CH_3); NMR ($CDCl_3$, 100 MHz) δ 0.74 (s, 3, CH_3), 0.81 (s, 3, CH_3), 0.95 (s, 3, CH_3). Anal. Calcd for $C_{15}H_{26}$: C, 88.16; H, 11.84. Found: C, 87.90; H, 12.02.

(3aα,4α,8aα)-Octahydro-3a,8,8a-trimethyl-4,8-methanoazulen-5(1*H*)-one (18).[30] To a stirred solution of MeLi (0.275 mL, 1.10 M, 0.300 mmol) in THF (5.0 mL) at −40 °C (dry ice/acetone) was added diisopropylamine (0.043 mL, 0.300 mmol) under N_2. After being stirred for 30 min, the solution was cooled to −78 °C (dry ice/acetone), and a solution of alcohol **15A** (0.100 g, 0.300 mmol) in THF (2.0 mL) was added. The resulting solution was allowed to warm to 0 °C (ice bath) over a period of 45 min, and then $ClPO(NMe_2)_2$ (0.0850 g, 0.058 mL, 0.500 mmol) was added. The reaction mixture was allowed to stir at room temperature for 20 h and then diluted with H_2O (25 mL) and worked up in the usual way to give 0.200 g of crude product. Chromatography on silica gel (30 g), using a solution of 1% MeOH–99% petroleum ether as an eluant, gave 0.087 g (62%) of pure phosphate ester: IR (CCl_4) 1670 cm^{-1} (C=C); NMR (CCl_4) δ 0.13 (s, 6, $SiMe_2$), 0.93 (s, 9, $SiCM_3$), 1.00 (s, 6, 2 CH_3), 1.15 (s, 6, CH_3), 2.03 (br s, 2, C=CHC**H**$_2$), 2.55, 2.72 (2 s, 12, 2 NMe_2), 4.43 (d, *J* = 9 Hz, 1, CHOP), 4.43 (m, 1, C=CH). A solution of this phosphate ester (0.087 g, 0.186 mmol) in Et_2O (5.0 mL) and *t*-BuOH (0.056 g) was added to a solution of Li metal (0.013 g, 1.90 mmol) in $EtNH_2$ (25 mL, double-distilled from Li) at −4 °C (ice–salt bath). After being stirred for 20 min at −4 to −2 °C, the reaction mixture was quenched with *t*-BuOH. The $EtNH_2$ was allowed to evaporate, and the residue was diluted with H_2O (25 mL) and worked up in the usual way to give 0.054 g of crude silyl enol ether. This material was dissolved in MeOH (5 mL), H_2O (0.5 mL), and Et_2O (3 mL) containing a catalytic amount of HCl gas. After 20 h at room temperature, the solution was diluted with water (20 mL) and worked up in the usual way to give 0.039 g of crude ketone **18**. Chromatography on silica gel (10 g), using a solution of 15% Et_2O–petroleum ether as an eluant, gave 0.023 g (61%) of ketone **18**: bp 50–60 °C (0.2 mmHg); IR 1710 cm^{-1} (C=O); NMR (CCl_4) δ 0.97 (s, 3, CH_3), 1.00 (s, 3, CH_3), 1.08 (s, 3, CH_3), 2.13 (s, 2, CH_2CO), 2.33 (m, 1, CHCO); low-resolution mass spectrum, *m/z* (relative intensity) 206 (m^+, 0.02), 110 (43), 109 (55), 96 (58), 95 (100), 94 (42), 81 (53), 79 (25), 67 (36), 55 (57), 53 (28), 41 (72). Anal. Calcd for $C_{14}H_{22}O$: *m/e* 206.1671. Found: *m/e* 206.1670 (mass spectrum), 0.5-ppm error (by high-resolution mass spectroscopy).

(±)-Gymnomitrene (2B).[29] Sodium hydride (0.056 g, 61.14%, 1.40 mmol) was washed with Et_2O (5.0 mL) and flushed with N_2. Triply distilled Me_2SO (3.0 mL) was added, and the mixture was heated at 80 °C for 30 min. The solution was cooled to room temperature, Ph_3PCH_3Br (0.500 g, 1.40 mmol) was added, and the resulting mixture was stirred at room temperature for 10 min. Ketone **18** (0.0130 g, 0.070 mmol) dissolved in Me_2SO (3.0 mL) was added, and the resulting solution was heated at 75 ± 2 °C for 20 h. The reaction was cooled to room temperature, diluted with H_2O (25 mL), and worked up in the usual way to give 0.030 g of crude product. Chromatography on silica gel (10 g) using petroleum ether as an eluant gave 0.0122 g (96%) of (±)-gymnomitrene (**2B**): IR (CCl_4) 3060, 1635, 860, 885 cm^{-1} (C=CH_2); NMR (CCl_4, 60 MHz) δ 0.84 (s, 3, CH_3), 0.91 (s, 3, CH_3), 1.04 (s, 3, CH_3), 4.50 (br s, 2, C=CH_2); NMR ($CDCl_3$, 100 MHz) δ 0.86 (s, 3, CH_3), 0.91 (s, 3, CH_3), 1.05 (s, 3, CH_3), 4.57 (br s, 2, C=CH_2); low-resolution mass spectrum, *m/z* (relative intensity) 204 (m^+, 0.02), 108 (75), 96 (84), 95 (62), 94 (54), 93 (87), 91 (32), 81 (68), 79 (43), 55 (47), 41 (67). Anal. Calcd for $C_{15}H_{24}$: *m/e* 204.1878. Found: *m/e* 204.1879 (mass spectrum), 0.5-ppm error (by high-resolution mass spectroscopy).

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Registry No. (±)-**2A**, 71564-38-0; (±)-**2B**, 72346-55-5; (±)-**3**, 74645-85-5; (±)-**4A**, 32854-37-8; (±)-**4B**, 72312-14-2; (±)-**4C**, 74629-79-1; **5A**, 74629-80-4; **5B**, 74629-81-5; **5C**, 74629-82-6; *cis*-**6**, 32139-03-0; (±)-**7**, 72312-15-3; (±)-**8**, 72312-16-4; (±)-**9** (isomer 1), 72312-18-6; (±)-**9** (isomer 2), 72312-17-5; (±)-**10**, 72312-19-7; (±)-**11A**, 74629-83-7; (±)-**11B**, 74629-84-8; **12**, 72312-20-0; (±)-**13**, 72312-21-1; (±)-**13** acid, 72312-04-0; (±)-**14B**, 72312-22-2; (±)-**15A**, 72312-23-3; (±)-**15A** bis(dimethylamino)phosphate ester, 74629-85-9; (±)-**15B**, 74708-12-6; (±)-**16** (R′ = $C(CH_3)_2OCH_3$), 72312-24-4; (±)-**17**, 74708-13-7; (±)-**18**, 72346-56-6; 2,3-dibromopropene, 513-31-5; propargyl bromide, 106-96-7; allyl chloride, 107-05-1; allyl bromide, 106-95-6; 2-methoxypropene, 116-11-0.

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