Total Synthesis of Sericenine

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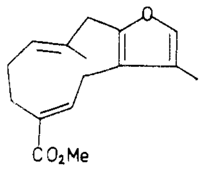
The total synthesis of the furanogermacrane sesquiterpene sericenine (**1**) is described. The key intermediate tetralone **6** was synthesized from (3,4-dimethoxyphenyl)acetonitrile (**7**) in four steps. Carbomethoxylation of **7** gave ester **8** which on conjugate addition with methyl acrylate gave diester **9**. Diester **9** was hydrolyzed and decarboxylated with KOH to give diacid **10**. Treatment of **10** with anhydrous HF gave the cyclodehydration product **6** in high overall yield. Reductive C-alkylation of **6** gave the two diasteromeric esters **4** and **5**. Stereospecific reduction of ketone **5** with $NaBH_4$ followed by acidic hydrolysis of the methyl enol ether gave the β-alcohol **11**. Hydrogenation of **11** with palladium-on-carbon gave exclusively the trans isomer **12**. Treatment of **12** with *p*-toluenesulfinyl chloride and subsequent oxidation with MCPBA gave the tosylate **3**. Aldol condensation of the generated zinc enolate of **3** with 1-[(tetrahydropyranyl)oxy]-2-propanone gave adduct **13**, which on treatment with *p*-toluenesulfonic acid in hot aqueous THF gave the furan **2**. Grob fragmentation of **2** using potassium bis(trimethylsilyl)amide in dry THF gave sericenine (**1**) in 43% yield from **2**. We conclude that the (*Z*,*E*)- instead of the (*E*,*E*)-1,5-cyclodecadiene ring was produced, because the intermediate trans dienolate iv is of lower energy than iii and sericenine is therefore the thermodynamically favored product.

A number of approaches to the synthesis of germacrene sesquiterpenes have been reported.[2] In our desire to synthesize complex germacrene sesquiterpenes, we and others have reported that the reductive alkylation of α-tetralone derivatives leads to suitably functionalized decalins which after functional group interconversion would on Grob fragmentation give the required germacrene skeleton.[3] In this paper we successfully use such an approach to synthesize the furanogermacrane sesquiterpene sericenine (1).[4]



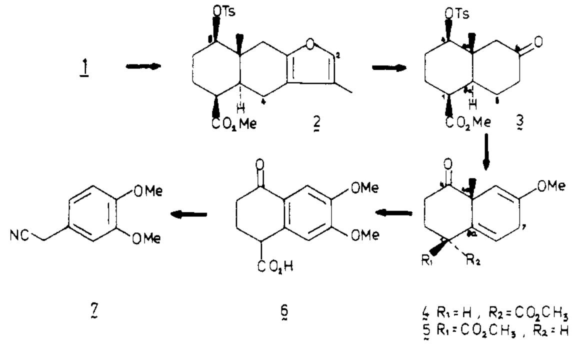
1 Sericenine

Sericenine (**1**) is a constituent of the essential oil of the leaves of *Neolitsea sericea* Koidz (Lauraceae) which grows in the southern parts of Japan and China.[4] The structure and conformation of **1** was properly elucidated by Takeda and co-workers.[5,6]

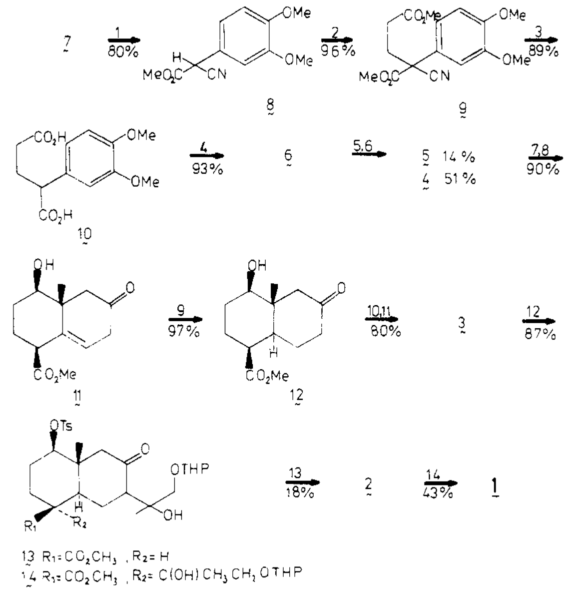
Results and Discussion

At the outset of this research we considered **3** as a key intermediate for the synthesis of sericenine (**1**) (Scheme I). The ketone of **3** at C-6 allows for 3-methylfuran annulation by the procedure of Hagiwara,[7] while the α- or β-methoxycarbonyl group at C-1 and the β-tosyl group at C-4 allow for the correct stereochemical requirements[8] for base-initiated Grob fragmentation to occur. The key compound **5** from which **3** could be obtained was synthesized by reductive alkylation of **6**.[3]

Scheme I



Scheme II[a]



[a] (1) NaH, $(MeO)_2CO$; (2) Triton B, $H_2C{=}CHCO_2Me$, MeOH; (3) KOH, aqueous MeOH; (4) HF; (5) KO-*t*-Bu, *t*-BuOH, K, NH_3, LiBr, THF, then aqueous THF, MeI; (6) CH_2N_2, Et_2O; (7) $NaBH_4$, EtOH; (8) $(CO_2H)_2$; (9) H_2, Pd/C, EtOH; (10) C_5H_5N, C_7H_7SOCl, CH_2Cl_2; (11) MCPBA, CH_2Cl_2; (12) *i*-Pr_2NLi, $ZnCl_2$, $MeCOCH_2OTHP$, THF; (13) *p*-TsOH, aqueous THF; (14) $KN(SiMe_3)_2$, THF.

Hence, we set about the synthesis of **6** starting with commerically available (3,4-dimethoxyphenyl)acetonitrile

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[1] University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.

(2) (a) "The Total Synthesis of Natural Products"; ApSimon, J., Ed.; John Wiley and Sons: New York, 1983; Vol. V, p 114 and references cited therein. (b) Kitahara, T.; Mori, K. *J. Org. Chem.* **1984**, *49*, 3281 and references cited therein.

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(4) (a) Hayashi, S.; Hayashi, N.; Matsuura, T. *Tetrahedron Lett.* **1968**, 1999. (b) Hayashi, N. *J. Sci. Hiroshima Univ., Ser. B, Div. 2*: **1969**, *33*, 107.

(5) Takeda, K.; Tori, K.; Horibe, I.; Minato, H.; Hayashi, N.; Hayashi, S.; Matsuura, T. *J. Chem. Soc. C* **1970**, 985.

(6) Tori, K.; Horibe, I.; Minato, H.; Takeda, K. *Tetrahedron Lett.* **1971**, 4355.

(7) Hagiwara, H.; Uda, H.; Kodama, T. *J. Chem. Soc., Perkin Trans. 1* **1980**, 963.

(8) Grob, C. A.; Kiefer, H. R.; Lutz, H.; Wilkens, H. *Tetrahedron Lett.* **1964**, 2901.

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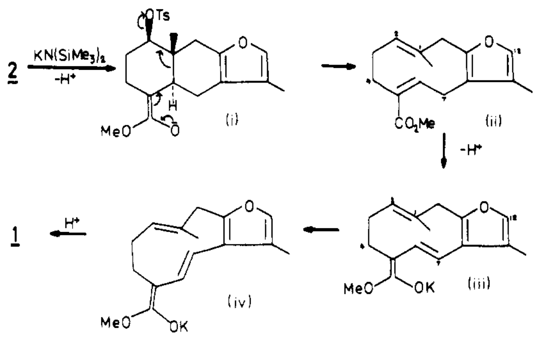
(**7**).[9] Carbomethoxylation of **7** with dimethyl carbonate and NaH gave ester **8** in high yield (Scheme II). Conjugate addition of the generated carbanion of **8** with methyl acrylate gave diester **9** which on hydrolysis of subsequent decarboxylation in refluxing methanolic KOH gave the diacid **10** in excellent overall yield. Cyclodehydration of **10** with anhydrous HF[10] gave tetralone **6** in 93% yield, mp 162–164 °C (lit.[3] mp 160–161 °C). The efficiency of this intramolecular acylation can be accounted by the electron-donating ability of the *p*-methoxy group of **10** which aids in the ring closure.

Reductive C-alkylation of **6** followed by esterification with diazomethane gave the two diastereomeric esters **4** (51%) and **5** (14%). Characteristic of this reductive alkylation reaction are the regiospecific protonation at C-7, brought about by using potassium and *tert*-butyl alcohol at low temperature, and regiospecific alkylation at C-4a via the lithium enolate.[3,11] The stereochemistry of **4** and **5** were were determined on the basis of ^{1}H NMR decoupling experiments. The theoretical allylic coupling angles $\theta_{8,1}$ as measured from Dreiding models for **4** and **5** are 100° and 15°, respectively. These values agreed with the measured H-8,1 coupling constants in the ^{1}H NMR for **4** ($J_{8,1}$ = 1.8 Hz) and **5** ($J_{8,1}$ = 0.8 Hz).[12]

As previously indicated, the stereochemistry of the C-1 methoxycarbonyl group is irrelevant since both configurations would give rise to a planar ester enolate, and Grob fragmentation can occur.[8] For convenience in our synthesis, we used β-ester **5** since hydrogenation of the α-ester equivalent of **11** gives both *trans*- and *cis*-decalins.[13] Sodium borohydride reduction of **5** followed by hydrolysis of the methyl enol ether with 0.5 M oxalic acid gave exclusively the equatorial alcohol **11** as evidenced by a sharp doublets of doublets of H-4 at δ 3.54 ($J_{4,3}$ = 11.2 Hz, $J_{4,3'}$ = 4.8 Hz) reflecting the diaxial and axial–equatorial couplings to the adjacent methylene protons at C-3.[15] Hydrogenation of **11** with palladium-on-carbon is stereospecific, giving only the trans isomer **12**. The stereochemistry at the ring junction was established by close comparison of the ^{1}H NMR chemical shift of the C-4a angular methyl group with those of similar decalin derivatives of known stereochemistry.[16] Tosylation of the sterically hindered alcohol of **12** with *p*-toluenesulfinyl chloride followed by oxidation of the sulfinate ester with MCPBA[17] gave **3** in 80% yield. Aldol condensation of the generated zinc enolate of **3** with 1-[(tetrahydropyranyl)oxy]-2-propanone[7] gave adduct **13** (52%) as well as dialkylated adduct **14** (35%). Attempts to minimize the yield of **14** were unsuccessfull. Treatment of **13** with a catalytic amount of *p*-toluenesulfonic acid in aqueous THF (60 °C, 0.5 h) furnished the furan **2** as an unstable oil. Grob fragmentation of **2** using potassium bis(trimethylsilyl)amide in dry THF (25 °C, 1 h) gave sericenine (**1**), mp 111–114 °C (lit.[4] mp 115 °C) in 43% yield. Sericenine (**1**) was spectroscopically identified by comparison with the natural compound.[4]

Scheme III



The interesting observation that only the (*Z*,*E*)-1,5-cyclodecadiene ring had been produced led us to the following mechanistic rationale (Scheme III). Proton abstraction at C-5 of **2** leads to the ester enolate (i) which undergoes concerted Grob fragmentation to give presumably neosericenine (ii); (a known natural product).[18] Abstraction of a proton at C-7 of ii with the excess base present leads to the cis ester dienolate (iii) which inverts giving the trans ester dienolate (iv) and on protonation at C-7 gives sericenine (**1**). Careful examination of Dreiding models of the conformations of iii and iv show noticably greater steric interactions between H-6 with H-2 and CH$_3$-14 and greater ring strain for iii then for iv. We can, therefore, presume that iv is the lower energy intermediate and that sericenine (**1**) is the thermodynamically favored product.

Experimental Section

Melting points were determined on a Büchi apparatus and are uncorrected. Infrared (IR) spectra were obtained with either a Perkin-Elmer 177 or 983 infrared spectrometer. Nuclear magnetic resonance spectra (NMR) were obtained with either a Varian T-60, JEOL JNM-PMX 60S1, or Varian XL-200 spectrometer in CDCl$_3$. Chemical shifts are reported in δ values relative to Me$_4$Si as the internal standard. Mass spectra were obtained on a VG 7070F high-resolution mass spectrometer. Microanalyses were performed by the University College Microanalytical Laboratory. Analytical thin-layer chromatography (TLC) was done on Merck 5719 glass backed silica gel 60F-254 precoated plates (thickness 0.25 mm). Compounds were visualized with either UV illumination, 10% phosphomolybdic acid in ethanol, or acidic ceric sulfate spray. Flash chromatography[19] was done with Merck silica gel 60 (230–400 mesh) and column chromatography with Fisons silica gel (80–200 mesh). Dry tetrahydrofuran (THF) was obtained by distillation over sodium benzophenone ketyl and dry dichloromethane by distillation over lithium aluminum hydride. Most of the commercial chemicals used were purified or dried by standard procedures.[20] All reactions were routinely carried out under an inert atmosphere of nitrogen.

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[9] Aldrich Chemical Co. Ltd.

[10] Hey, D. H.; Nagdy, K. A. *J. Chem. Soc.* **1953**, 1894.

[11] Narisada, M.; Watanabe, F. *J. Org. Chem.* **1973**, *38*, 3887.

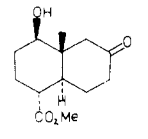
[12] Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry"; Pergamon Press: Oxford, 1969; Vol. V, p 316.

[13] (a) Results to be published in the synthesis of several eudesmane sesquiterpenes. (b) Attempted isomerization of the double bond to the enone with RhCl$_3$·3H$_2$O[14] also gave cis (22%) and trans (30%) ring junctions as well as some isomerization to C1–C8a.

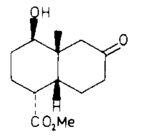
[14] Grieco, P. A.; Nishizawa, M.; Marinovic, N. *J. Am. Chem. Soc.* **1976**, *98*, 7102.

[15] It would be expected to give the equatorial alcohol product due to NaBH$_4$ approaching the sterically less hindered α-face of **11**.

[16] For example, ^{1}H NMR for A (δ = 0.77), B (δ = 1.14), and **12** (δ = 0.76) for 4a-CH$_3$. The structure of A was determined by X-ray crystallographic analysis.



A



B

[17] Coates, R. M.; Chen, J. P. *Tetrahedron Lett.* **1969**, 2705.

[18] (a) Takeda, K.; Horibe, I.; Minato, H. *J. Chem. Soc. C* **1970**, 1547. (b) The physical properties and spectral data for neosericenine are very much more different to those for sericenine.[4–6]

[19] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

[20] Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. "Purification of Laboratory Chemicals"; Pergamon Press: Oxford, 1980.

Methyl 2-(3,4-Dimethoxyphenyl)-2-cyanoethanoate (8). A portion (100 mL) of (3,4-dimethoxyphenyl)acetonitrile (7) 50 g, 0.28 mol) in dimethyl carbonate (300 mL) was added to a stirred solution of NaH (22 g, 0.92 mol) in dry THF (200 mL) at 25 °C under N_2. After 5 min, the remainder of 7 was added over a period of 30 min. After 1.5 h, the mixture was stirred at reflux for 18 h. Water was added to the cooled mixture, and this was washed once with Et_2O to remove the excess dimethyl carbonate. The aqueous layer was separated and acidified with 2 N HCl and the product was extracted with Et_2O. The combined extracts were washed with water and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo followed by recrystallization from EtOAc afforded 52.6 g (80%) of the ester **8** as colorless crystals: mp 91–93 °C (EtOAc); IR (Nujol) 2980, 2280, 1760, 1620, 1610, 818 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.82 (s, 3 H, CO_2CH_3), 3.90 and 3.92 (two s, 3 H each, two OCH_3), 4.70 (s, 1 H, C*H*CNCO$_2$Me), 6.86–7.04 (m, 3 H, Ar); MS, M^+ 235.0833, calcd for $C_{12}H_{13}NO_4$ 235.0844. Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.96. Found: C, 61.16; H, 5.59; N, 6.09.

Dimethyl 2-(3,4-Dimethoxyphenyl)-2-cyanopentanedioate (9). A solution of methyl acrylate (30.3 mL, 0.34 mol) in MeOH (20 mL) was added dropwise to a stirred solution of ester **8** (35 g, 0.15 mol) in MeOH (80 mL) at 40 °C under N_2. After the addition of several drops of methyl acrylate, benzyltrimethylammonium hydroxide (Triton B,[21] 1 mL) was added, and an additional portion of Triton B (1 mL) was added after half of the methyl acrylate had been added to the reaction mixture. On completion of the addition of methyl acrylate, 0.5 h, the mixture was further stirred at 40 °C for 24 h. The cooled reaction mixture was diluted with water and acidified with 1 N HCl and extracted with Et_2O. The combined extracts were washed with water and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo followed by recrystallization from EtOAc gave the diester **9** (46 g, 96%) as colorless crystals: mp 65–67 °C (EtOAc); IR (Nujol) 2850, 2260, 1745, 1600, 1520, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40–2.52 (m, 4 H, $CH_2CH_2CO_2Me$), 3.71 and 3.84 (two s, 3 H each, two CO_2CH_3), 3.94 and 3.96 (two s, 3 H each, two OCH_3), 6.87–7.16 (m, 3 H, Ar); MS, M^+ 321.1219, calcd for $C_{16}H_{19}NO_6$ 321.1212. Anal. Calcd for $C_{16}H_{19}NO_6$: C, 59.80; H, 5.96; N, 4.36. Found: C, 59.80; H, 5.91; N, 4.25.

2-(3,4-Dimethoxyphenyl)pentanedioic Acid (10). The diester **9** (38 g, 0.12 mol) in a solution of KOH (74.5 g), MeOH (75 mL), and water (75 mL) was stirred at reflux for 24 h. The reaction mixture was cooled and acidified with 2 N HCl and extracted with EtOAc. The combined extracts were washed with water and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo followed by recrystallization from EtOAc gave the diacid **10** (28.65 g, 89%) as colorless needles: mp 156–157 °C (EtOAc); IR (Nujol) 1700, 1610, 1525, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.12–3.00 (m, 5 H), 3.87 (s, 6 H, two OCH_3), 6.78–7.24 (m, 3 H, Ar), 8.40 (br s, 2 H, two CO_2H); MS, M^+ 268.0952, calcd for $C_{13}H_{16}O_6$ 268.0947. Anal. Calcd for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 58.11; H, 6.02.

6,7-Dimethoxy-4-oxo-1,2,3,4-tetrahydro-1-naphthoic Acid (6). Anhydrous HF[10] (ca. 20 mL) was added to the diacid **10** (10.0 g, 37 mmol) in a polyethylene bottle cooled at 0 °C. After 4 h at room temperature, the remaining HF was evaporated by bubbling air through the solution, and then ice-cold water was added. The residual solid was extracted with CH_2Cl_2 and repeatedly washed with water and brine and then dried over $MgSO_4$. Evaporation of the solvent in vacuo followed by recrystallization from EtOAc gave the tetralone **6** (8.62 g, 93%) as colorless needles: mp 162–164 °C (lit.[3] mp 160–161 °C) (EtOAc); IR (Nujol) 3520–3400 (br), 2920, 1710, 1670, 1595, 1365, 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40–3.02 (m, 5 H), 3.96 and 3.98 (two s, 3 H each, two OCH_3), 6.84 (s, 1 H, Ar), 7.60 (s, 1 H, Ar), 10.24 (s, 1 *H*, CO_2H); MS, M^+ 250.0828, calcd for $C_{13}H_{14}O_5$ 250.0841. Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.01; H, 5.59.

Methyl (1α,4aβ)-6-Methoxy-4a-methyl-4-oxo-1,2,3,4,4a,7-hexahydro-1-naphthoate (4) and Methyl (1β,4aβ)-6-Methoxy-4a-methyl-4-oxo-1,2,3,4,4a,7-hexahydro-1-naphthoate (5). To a stirred solution of **6** (10.0 g, 40 mmol) and *tert*-butyl alcohol (8.9 g, 120 mmol) in dry THF (50 mL) was added potassium *tert*-butoxide (4.9 g, 44 mmol) at −78 °C under N_2. Dry ammonia (500 mL) was then added, followed by pieces of potassium metal (7.8 g, 200 mmol). After 10 min, a solution of dry LiBr (17.2 g, 200 mmol) in dry THF (50 mL) was added, followed by (after 15 min) the simultaneous addition of MeI (17.5 mL, 280 mmol) and aqueous THF (1:1, 100 mL). The cooling bath was removed and the ammonia driven off by using a warm water bath. The mixture was cooled at −10 °C and acidified with 2 N HCl (also cooled at −10 °C) to pH 10. Then CH_2Cl_2 (300 mL) was added, and with vigorous cooling and swirling, the acidification was carefully continued until the solution was at pH 3. The organic extract was separated and the aqueous layer back-extracted with CH_2Cl_2. The combined extracts were washed with water and brine, filtered (Whatman No. 1 PS), and treated with an excess of ethereal diazomethane (64 mmol), stirring at −10 °C for 0.5 h. Then N_2 was bubbled for 0.5 h through the solution to expel any remaining diazomethane. Evaporation of the solvent in vacuo gave a crude mixture of **4** and **5** which on trituration with EtOAc–petroleum ether (3:7) gave a portion of the pure α-ester **4**. Flash chromatography of the mixture (Et_2O–petroleum ether, 3:7) gave the remaining α-ester **4** (total yield: 5.14 g, 51%) as colorless crystals and the β-ester **5** (1.72 g, 14%) as colorless crystals.

α-Ester 4: mp 123–125 °C (EtOAc–pentane) (lit. mp 123–125 °C) IR (Nujol) 2970, 1742, 1715, 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (s, 3 H, 4a-CH_3), 1.93–2.54 (m, 4 H), 2.59 (dd, 1 H, J_{gem} = 21.1 Hz, $J_{7,8}$ = 3.3 Hz, 7-H), 2.67 (ddd, 1 H, J_{gem} = 21.1 Hz, $J_{7',8}$ = 4.1 Hz, $J_{7',5}$ = 1.0 Hz, 7′-*H*), 3.58 (s, 3 H, CO_2CH_3), 3.61–3.69 (m, 1 H, 1-H), 3.79 (s, 3 *H*, OCH_3), 4.94 (d, 1 H, $J_{5,7'}$ = 1.0 Hz, 5-H), 5.29 (ddd, 1 H, $J_{8,7'}$ = 4.1 Hz, $J_{8,7}$ = 3.3 Hz, $J_{8,1}$ = 1.8 Hz, 8-H); MS, M^+ 250.1196, calcd for $C_{14}H_{18}O_4$ 250.1204. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 66.92; H, 7.44.

β-Ester 5: mp 89–90 °C (EtOAc–petroleum ether) (lit.[3] mp (89–90 °C); IR (Nujol) 2970, 1740, 1715, 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (s, 3 H, 4a-CH_3), 1.80–2.62 (m, 4 H), 2.71 (dd, 1 H, J_{gem} = 21.2 Hz, $J_{7,8}$ = 3.1 Hz, 7-H), 2.78 (ddd, 1 H, J_{gem} = 21.2 Hz, $J_{7',8}$ = 4.4 Hz, $J_{7',5}$ = 1.0 Hz, 7′-H), 3.44 (t, 1 H, J = 5.4 Hz, 1-H), 3.61 (s, 3 H, CO_2CH_3), 3.75 (s, 3 H, OCH_3), 4.95 (d, 1 H, $J_{5,7'}$ = 1.0 Hz, 5-H), 5.76 (ddd, 1 H, $J_{8,7'}$ = 4.4 Hz, $J_{8,7}$ = 3.1 Hz, $J_{8,1}$ = 0.8 Hz, 8-H); MS, *m/e* (relative intensity) 250 (24, M^+), 235 (4), 222 (4), 207 (6), 191 (52), 163 (base). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; 7.25. Found: C, 67.60; H, 7.25.

Methyl (1β,4β,4aβ)-4-Hydroxy-4a-methyl-6-oxo-1,2,3,4,4a,5,6,7-octahydro-1-naphthoate (11). Sodium borohydride (60 mg, 1.5 mmol) was added to a stirred solution of **5** (1.05 g, 4.2 mmol) in absolute ethanol (60 mL) at 0 °C under N_2. After 0.5 h, the reduction had gone to completion by TLC and 0.5 M oxalic acid (40 mL) was added, and the mixture was further stirred at room temperature for 0.5 h. The mixture was diluted with water (200 mL) and extracted with Et_2O. The combined extracts were washed with water and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo followed by recrystallization from CH_2Cl_2–petroleum ether gave 11 (895 mg, 90%) as colorless crystals: mp 118–120 °C (CH_2Cl_2–petroleum ether); IR (Nujol) 3280, 2980, 1745, 1725, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (d, 3 H, J = 0.8 Hz, 4a-CH_3), 1.44–1.99 (m, 4 H), 2.32 (dddd, 1 H, $J_{2',2}$ = 13.4 Hz, $J_{2',3}$ = 4.8 Hz, $J_{2',3'}$ = 3.2 Hz, $J_{2',1}$ = 1.6 Hz, 2′-H), 2.46 (d, 1 H, $J_{5,5'}$ = 13.2 Hz, 5-H), 2.66 (dd, 1 H, $J_{5',5}$ = 13.2 Hz, $J_{5',7}$ = 1.4 Hz, 5′-H), 2.85 (ddd, 1 H, J_{gem} = 21.6 Hz, $J_{7',8}$ = 3.7 Hz, $\mathrm{J}_{7',5'}$ = 1.4 Hz, 7′-H), 3.06 (dd, 1 H, J_{gem} = 21.6 Hz, $J_{7,8}$ = 3.7 Hz, 7-H), 3.20 (br d, 1 H, $J_{1,2}$ = 5.6 Hz, 1-H), 3.54 (dd, 1 H, $J_{4,3}$ = 11.2 Hz, $J_{4,3'}$ = 4.8 Hz, 4-H), 3.66 (s, 3 H, CO_2CH_3), 5.70 (dt, 1 H, $J_{8,7}$ = $\mathrm{J}_{8,7'}$ = 3.7 Hz, $J_{8,1}$ = 0.8 Hz, 8-H); MS, M^+ 238.1213, calcd for $C_{13}H_{18}O_4$ 238.1205. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.52; H, 7.73.

Methyl (1β,4β,4aβ,8aα)-4-Hydroxy-4a-methyl-6-oxo-1,2,3,4,4a,5,6,7,8,8a-decahydro-1-naphthoate (12). To 11 (1.7 g, 7.14 mmol) in absolute ethanol (200 mL) was added 10% palladium-on-carbon (236 mg). The whole system was evacuated of air and then filled with H_2. The procedure was repeated 3 times. With vigorous stirring for 2 h at room temperature, 11 was hydrogenated (using hydrogenation apparatus);[22] H_2 uptake (160 mL). The catalyst was removed by filtering the solution through a pad of Celite. Evaporation of the solvent in vacuo followed by

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[21] 40% w/v in methanol, Aldrich Chemical Co. Ltd.

[22] "Vogel's Textbook of Practical Organic Chemistry"; Longmans: London, 1978, p 65.

recrystallization from Et_2O gave **12** (1.66 g, 97%) as colorless needles: mp 93–94 °C (Et_2O); IR (CH_2Cl_2) 3600, 2920, 2870, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76 (d, 3 H, J = 1.0 Hz, 4a-CH_3), 1.36–2.60 (m, 13 H), 3.48 (dd, 1 H, $J_{4,3}$ = 11.2 Hz, $J_{4,3'}$ = 4.5 Hz, 4-H), 3.70 (s, 3 H, CO_2CH_3); MS, M^+ 240.1364, calcd for $C_{13}H_{20}O_4$ 240.1361. Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.79; H, 8.38.

Methyl (1β,4β,4aβ,8aα)-4a-Methyl-6-oxo-4-[(*p*-tolylsulfonyl)oxy]-1,2,3,4,4a,5,6,7,8,8a-decahydro-1-naphthoate (3). To a stirred solution of **12** (500 mg, 2.08 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C under N_2 was added anhydrous pyridine (0.33 mL, 4.1 mmol) followed by *p*-toluenesulfinyl chloride[23] (0.38 mL, 4.1 mmol). The mixture was stirred for 3 h at 0 °C, then poured into 1 N HCl, and extracted with CH_2Cl_2. The combined extracts were washed with 5% $NaHCO_3$ solution, water, and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo gave a mixture of diastereomeric sulfinate esters (786 mg) as a colorless oil: IR (CH_2Cl_2) 2870, 1705, 1130, 1115, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76 and 0.78 (2 s, 3 H, 4a-CH_3), 1.28–2.40 (m, 11 H), 2.42 (s, 3 H, $ArCH_3$), 2.54–2.68 (m, 1 H, 1-H), 3.67 and 3.70 (2 s, 3 H, CO_2CH_3), 4.09 and 4.20 (2 dd, 1 H, J = 4.40, 12.2 Hz, 4-H), 7.38 and 7.65 (2 d, 2 H each, J = 8.0 Hz, Ar). To a stirred solution of the crude sulfinate ester (786 mg, 2 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C under N_2 was added *m*-chloroperbenzoic acid (500 mg, 2.9 mmol). After having been stirred for 3 h at 0 °C, the mixture was poured into saturated $NaHCO_3$ solution, washed with water and brine, and dried over $MgSO_4$. Evaporation of the solvent in vacuo and purification of the residue by flash chromatography (PhH–Et_2O–petroleum ether, 1:2:2) gave the tosylate **3** (656 mg, 80%) as colorless crystals: mp 153–154 °C (Et_2O); IR (CH_2Cl_2) 2850, 1725, 1355, 1180, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.78 (s, 3 H, 4a-CH_3), 1.54–2.40 (m, 11 H), 2.46 (s, 3 H, $ArCH_3$), 2.54–2.64 (m, Hz, H, 1-H), 3.68 (s, 3 H, CO_2CH_3), 4.45 (dd, 1 H, J = 4.40, 12.18 Hz, 4-H), 7.40 and 7.84 (two d, 2 H each, Ar); MS, *m/e* (relative intensity) 394 (7, M^+), 239 (12), 223 (base), 222 (30), 207 (44). Anal. Calcd for $C_{20}H_{26}O_6S$: C, 60.89; H, 6.64; S, 8.13. Found: C, 60.70; H, 6.61; S, 8.05.

Methyl (1β,4β,4aβ,8aα)-4a-Methyl-6-oxo-7-[2-hydroxy-3-[(tetrahydropyranyl)oxy]propanyl]-1,2,3,4,4a,5,6,7,8,8a-decahydro-1-naphthoate (13). To a stirred solution of LDA (0.97 mmol) in dry THF (2 mL) at −78 °C under N_2 was added dropwise a solution of **3** (175 mg, 0.44 mmol) in dry THF (4 mL). After 0.5 h, anhydrous zinc chloride (137 mg, 1.01 mmol) in dry THF (2 mL) was added. After another 5 min, 1-[(tetrahydropyranyl)oxy]-2-propanone[7] (153 mg, 0.97 mmol) in dry THF (1 mL) was added, and the stirring was continued at −78 °C for 0.5 h and then at −20 °C for 1 h. Aqueous NH_4Cl solution was added, and the product was extracted with Et_2O. The combined extracts were washed with water and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo followed by flash chromatography (PhH–Et_2O–CH_2Cl_2, 2:2:1) of the residue gave unreacted **3** (17 mg, 10%), the THP adduct **13** (121 mg, 52%), and the dialkylated adduct **14** (109 mg, 35%), both as colorless oils. THP adduct **13**: IR (CH_2Cl_2) 3500, 2940, 2870, 1705, 1695, 1360, 1180, 840, 820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.73, 0.76, 0.86, 0.89 (4 s, CH_3), 1.22 and 1.27 (2 s, R′(CH_3)CHOHR″), 1.56–2.30 (m, 18 H), 2.47 and 2.48 (2 s, $ArCH_3$), 3.34–3.94 (s overlapping m, 7 H, CO_2CH_3 and THP), 4.41 (dd, 1 H, J = 4.38, 12.20 Hz, 4-H), 4.54–4.72 (m, 2 H, R′(Me)CHOHR″ and THP), 7.38 and 7.82 (2 d, 2 H each, J = 8.0 Hz, Ar); MS, *m/e* (relative intensity) 506 (0.1, M − CH_3), 190 (3), 172 (62), 155 (7), 108 (25), 107 (33), 91 (base). Dialkylated adduct **14**: IR (CH_2Cl_2) 3500, 2930, 2860, 1725, 1360, 1180, 840, 820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82–0.96 (m, CH_3), 1.08–1.40 (m, 6 H, two CH_3), 1.44–2.40 (m, 24 H), 2.47 and 2.56 (2 s, $ArCH_3$), 3.30–3.93 (s overlapping m, 11 H, CO_2CH_3 and THP), 4.40–4.72 (m, 5 H, R′(Me)CHOHR″, THP, and 4-H), 7.34–7.50 (m, 2 H, Ar), 7.70–7.94 (m, 2 H, Ar).

(4aα,5β,8β,8aβ)-5-(Methoxycarbonyl)-3,8a-dimethyl-8-[(*p*-tolylsulfonyl)oxy]-4,4a,5,6,7,8,8a,9-octahydronaphtho[2,3-*b*]furan (2). A stirred solution of **13** (40 mg, 0.08 mmol) in THF–H_2O (2:1, 1.5 mL) containing a catalytic amount of *p*-toluenesulfonic acid (1 mg) was heated at 60 °C for 0.5 h. The solution was cooled and poured into aqueous $NaHCO_3$ solution, and the product was extracted with Et_2O. The combined ethereal extracts were washed with water and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo, followed by immediate flash chromatography (CH_2Cl_2), gave the furan **2** (6 mg, 18%) as a colorless oil which is unstable and decomposes slowly on standing at room temperature: IR ($CHCl_3$) 2933, 2845, 1729, 1597, 1175, 1019, 940 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (s, 3 H, 8a-CH_3), 1.91 (d, 3 H, J = 1.16 Hz, C3-CH_3), 1.55–2.66 (m, 10 H), 2.46 (s, 3 H, $ArCH_3$), 3.69 (s, 3 H, CO_2CH_3), 4.44 (dd, 1 H, J = 4.41, 12.16 Hz, 8-H), 7.01 (br s, 1 H, 2-H), 7.40 and 7.86 (2 d, 2 H each, J = 8.0 Hz, Ar); MS, *m/e* (relative intensity) 432 (11, M^+), 261 (2), 260 (6), 155 (31), 108 (57), 91 (base).

Sericenine (1). To the furan **2** (12 mg, 0.03 mmol) in dry THF (1 mL) was added potassium bis(trimethylsilyl)amide in THF (0.06 mL, 0.06 mmol). After stirring for 1 h at 25 °C under N_2, the reaction had gone to completion by TLC. The mixture was poured into water and extracted with Et_2O. The ethereal extracts were washed with water and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo followed by flash chromatography (CH_2Cl_2–petroleum ether, 3:7) of the residue gave **1** as white needles (3 mg, 43%): mp 111–114 °C (lit.[4] mp 115 °C); IR ($CHCl_3$) 3040, 1706, 1640, 1550 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (br s, 3 H, 14-CH_3), 1.97 (d, 3 H, J = 1.16 Hz, 13-CH_3), 2.2–2.64 (m, 4 H), 2.78–2.94 (m, 1 H, 7-βH), 3.15 and 3.54 (2 d, 1 H each, J = 14.7 Hz, 10β, 10α-H), 3.52–3.66 (br d, 1 H, 7α-H), 3.73 (s, 3 H, CO_2CH_3), 5.50 (t, 1 H, J = 7.5 Hz, 2-H), 6.63 (br d, 1 H, 6-H), 7.06 (br s, 1 H, 12-H); MS, *m/e* (relative intensity) 260 (45, *M^+*), 245 (11), 229 (6), 201 (19), 108 (base), *m/e* calcd for $C_{16}H_{20}O_3$ 260.1412, found 260.1422. Comparison of the IR, ^1H NMR, and MS with the corresponding spectra of natural sericenine[4] was identical.

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[23] Kurzer, F. "Organic Synthesis", John Wiley and Sons: New York, 1963; Collect. Vol. 4, p 937.

Ultrasound in Phosphine Preparation. Simple Preparations of Some Bis(alkylphenylphosphino)alkanes

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Diphosphines of the class $RPhP(CH_2)_nPPhR$ (n = 2–6) have been prepared from the reactions of the corresponding $Ph_2P(CH_2)_nPPh_2$ with alkali metal followed by alkylation. Ultrasound irradiation should be applied in the reductive cleavage stage so as to assure the purity of the final products.

Diphosphines of the general type $PhRP(CH_2)_nPRPh$ are important chelating reagents for the preparation and mechanistic study of various transition-metal complexes and catalysts. The conventional method preparation in-

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