An Efficient Approach to Chiral, Nonracemic *trans*-Decahydro-5,8a-dimethyl-1,6-naphthalenedione Derivatives: Total Synthesis of (+)-Pallescensin A

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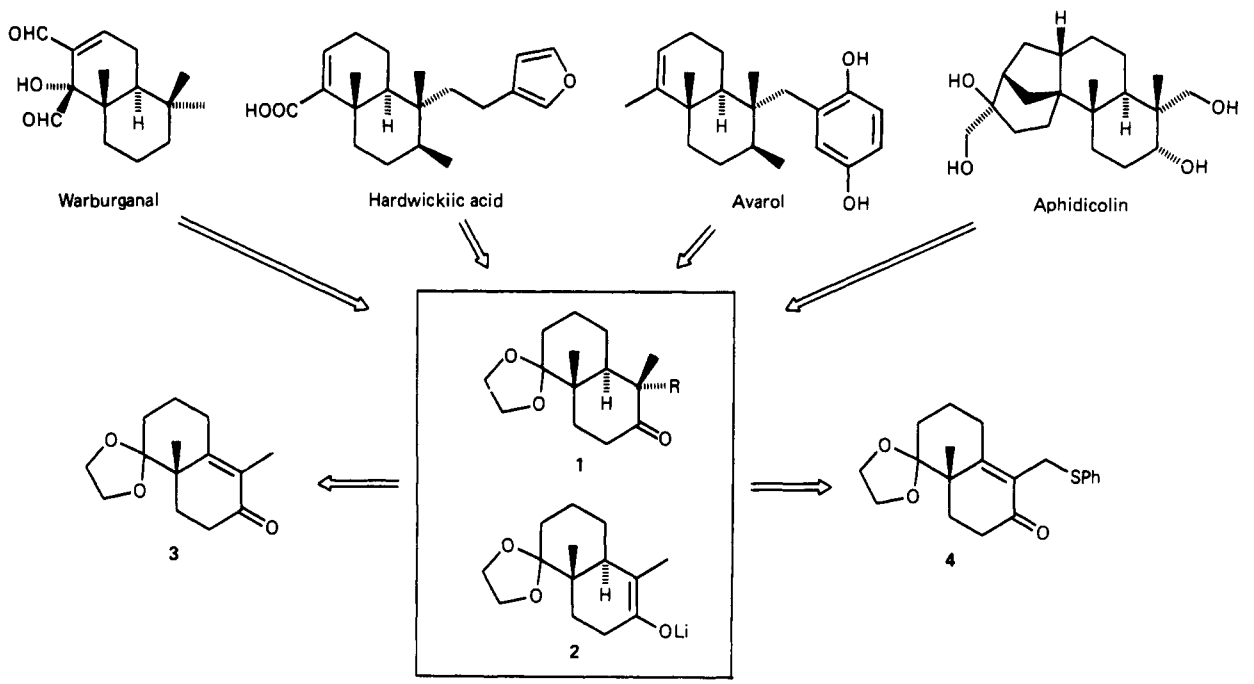
The syntheses of six chiral, nonracemic *trans*-decahydro-5,8a-dimethyl-1,6-naphthalenedione derivatives **1a–f** are described. The approach calls for the reductive alkylation of enone **4** readily available from (+)-Wieland–Miescher ketone (**5**) via chemoselective ketalization on the C(8)-carbonyl followed by application of the Kirk–Petrow (phenylthio)methylation protocol. Yields for reactive electrophiles are in the range of 70–85%. To demonstrate the utility of this method, we record here a nine-step total synthesis of (+)-pallescensin A (**8**); the overall yield from enone **4** was 13%.

As a group *trans*-decalones of the general type **1** have found considerable versatility in the construction of sesquiterpenes, diterpenes, and other architecturally complex natural products (e.g., warburganal,[2] hardwickiic acid,[3] avarol[4] and aphidicolin[5]). However, a convenient method for the preparation of such intermediates in chiral, nonracemic form is not available.[6] That is, while a variety of *trans*-decalones can be prepared via alkylation of enolate **2**, available via lithium–liquid ammonia reduction of enone **3**,[7] a convenient method for the preparation of **3** in high yield and in high optical purity was not available[8] at the outset of this work (Scheme I).

In considering an approach that would provide enolate **2** in chiral, nonracemic form, we were attracted to enone **4** for three reasons. First, Coates and Sowerby[9] demonstrated that α-(*n*-butylthio)methylene ketones undergo efficient reductive alkylation. We anticipated that (phenylthio)methyl enone **4** would, in a similar fashion, lead to the desired enolate (i.e., **2**), which could then be captured with a variety of electrophiles. Second, enone **4** was envisioned to be readily available from optically pure Wieland–Miescher ketone,[10] via application of the Kirk–Petrow reaction.[11] Finally, it appeared that both operations would be amenable to large-scale work.

Scheme I



(1) Camille and Henry Dreyfus Teacher–Scholar, 1978–1983; National Institutes of Health (National Cancer Institute) Career Development Award, 1980–1985.

(2) (a) Kubo, I.; Lee, Y.-W.; Pettei, M.; Pilkiewicz, F.; Nakanishi, K. *J. Chem. Soc., Chem. Commun.* **1976**, 1013. (b) Kende, A. S.; Blacklock, T. J. *Tetrahedron Lett.* **1980**, *21*, 3119.

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(6) For a synthesis of a related *trans*-decalone in optically pure form, see: Dutcher, J. S.; Macmillan, J. G.; Heathcock, C. H. *J. Org. Chem.* **1976**, *41*, 2663.

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(9) Coates, R. M.; Sowerby, R. L. *J. Am. Chem. Soc.* **1971**, *93*, 1027.

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(11) Kirk, D. N.; Petrow, V. *J. Chem. Soc.* **1962**, 1091.

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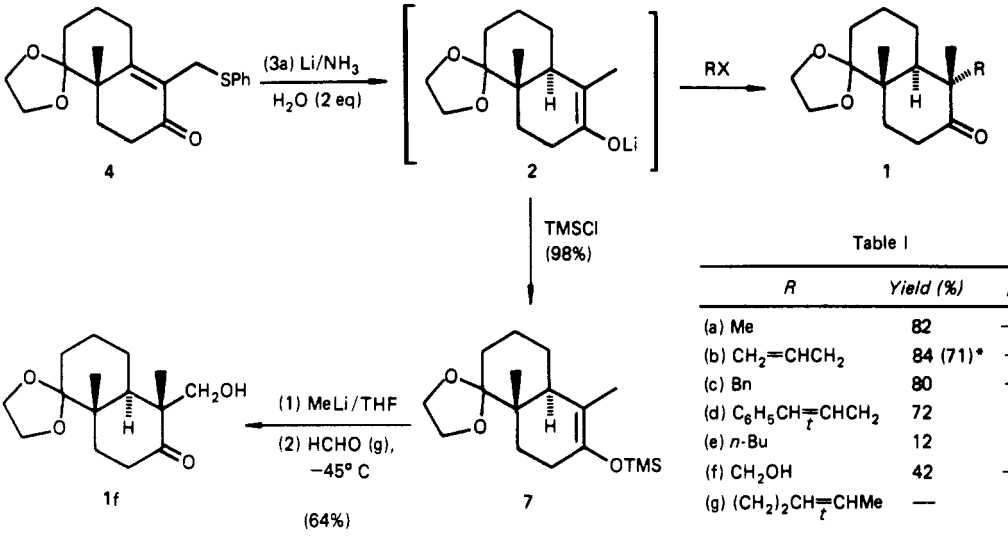
Scheme II



4 2 1 1f 7

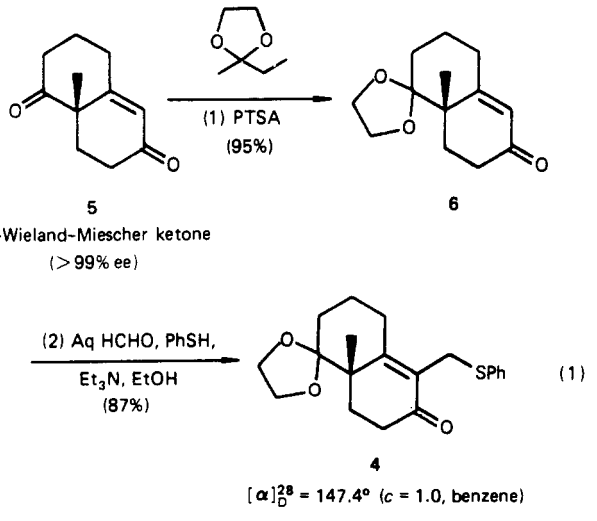
Table I

R	Yield (%)	$[\alpha]_D^{22}$
(a) Me	82	−35°
(b) $CH_2{=}CHCH_2$	84 (71)*	+27°
(c) Bn	80	+21°
(d) $C_6H_5CH{=}CHCH_2$	72	+7.4°
(e) *n*-Bu	12	+2.1°
(f) CH_2OH	42	−68°
(g) $(CH_2)_2CH{=}CHMe$	—	—

*Kuwajima protocol.[15]

In this, a full account, we report that the reductive alkylation of enone **4** is in fact an effective method for the preparation of a number of *trans*-decalones (**1a–d**) in chiral, nonracemic form. We note in advance that the synthetic sequence is economic (three steps from Wieland–Miescher), efficient (60–70% overall yield), and amenable to modest (if not large) scale preparations. To demonstrate the utility of this approach, we have successfully completed an enantioselective total synthesis of (+)-pallescensin A (**8**), a furanosesquiterpene first isolated by Cimino et al.[12] in 1975 from the marine sponge *Disidera pallescens*.

Reductive Alkylations. Enone **4**, substrate for the proposed reductive alkylation, was prepared from (+)-Wieland–Meischer ketone (**5**) available in >99% enantiomeric excess via the Hajos[10a]–Eder[10b] protocol (see eq 1). Chemoselective transketalization[13] employing the



5 6

(+)-Wieland-Miescher ketone
(>99% ee)

4

$[\alpha]_D^{28}$ = 147.4° (*c* = 1.0, benzene) (1)

ethylene ketal of 2-butanone and PTSA followed by treatment of the derived monoketal **6** with aqueous formaldehyde, thiophenol, and triethylamine in ethanol according to the protocol of Kirk and Petrow[11] led to enone **4** in 83% overall yield.

Reductive alkylations were then carried out in the following manner. Enone **4** and 2 equiv of water were added in THF to 3 equiv of lithium in liquid ammonia to generate enolate **2**. After a period of 20–30 min, sufficient additional THF was added to the reaction mixture to assure that the ratio of THF to ammonia was at least 1:3. If lower ratios of THF to ammonia are employed, inferior yields of alkylation result. Presumably enolate **2** is not completely solvated when the percentage of THF falls below 25%.[14] Addition of a variety of alkylating agents to enolate **2** led to the results recorded in Table I.

In general, reactive alkylating agents afforded good to excellent yields whereas less active electrophilic agents gave little or no reaction. In an attempt to circumvent the low reactivity of lithium enolates with less active electrophiles, we prepared the more reactive benzyltrimethylammonium enolate from trimethylsilyl enol ether **7** via the Kuwajima procedure.[15] Toward this end, enol silyl ether **7** prepared from **2** was treated at room temperature, respectively, with allyl bromide, *n*-butyl iodide, and *trans*-1-iodo-3-pentene (a homoallylic iodide) in the presence of benzyltrimethylammonium fluoride (BTAF). While allyl bromide afforded **1b** in 71% yield, *n*-BuI and *trans*-1-iodo-3-pentene gave no detectable alkylation. Thus only reactive electrophiles are suitable for the alkylation of enolates derived from **4**. A modest improvement in the yield of **1f** (64 vs. 42%) was obtained when the two-step procedure illustrated in Scheme II was employed. Finally, we note that the stereochemistries of the alkylation products **1a–f** were based either on comparison with literature spectra or on literature precident (see Experimental Section).

(+)-Pallescensin A (8). To illustrate in natural product synthesis the synthetic utility of the above reductive alkylation protocol, we completed an enantioselective total synthesis of the furanosesquiterpene (+)-pallescensin A (**8**). We note that pallescensin has been prepared previously in both racemic[16] and chiral forms;[17]

(12) Cimino, G.; DeStefano, S.; Guerriero, A.; Minale, L. *Tetrahedron Lett.* **1975**, 1425.
(13) Baudin, G.; Pietrasanta, Y. *Tetrahedron* **1973**, *29*, 4225.
(14) Stork, G.; Rosen, P.; Goldman, N.; Coombs, R. V.; Tsuji, J. *J. Am. Chem. Soc.* **1965**, *87*, 275.
(15) Kuwajima, I.; Nakamura, E. *J. Am. Chem. Soc.* **1975**, *97*, 3257.
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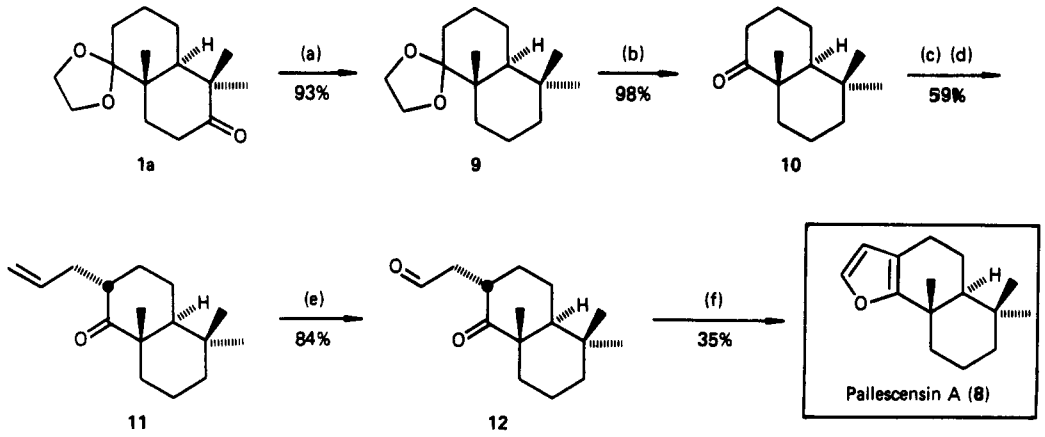
Scheme III[a]



[a] (a) KOH, trimethylene glycol, H_2NNH_2, 190°; (b) 3 N HCl, THF; (c) (1) LDA, Me_3SiCl, (2) $PhCH_2NMe_3F$, $BrCH_2CH{=}CH_2$, (d) K_2CO_3, MeOH; (e) (1) O_3, (2) PPh_3; (f) $BF_3{\cdot}Et_2O$, benzene, Dean-Stark.

however, the syntheses in general are either quite long, low yielding, nonstereoselective, and/or afford pallescensin A (8) in low enantiomeric purity.

Our strategy, illustrated in Scheme III, begins with decalone **1a**, prepared as described above in 68% overall yield from (+)-Wieland–Miescher ketone. Wolff–Kishner reduction[20] followed by hydrolysis of the ketal functionality afforded ketone **10** in 91% yield for the two steps.

Turning next to construction of the furan ring, we encountered two unanticipated difficulties. First, all attempts to alkylate **10** by employing the now standard lithium amide base technology led to complex mixtures of unalkylated, monoalkylated, and dialkylated ketones. To circumvent this problem we again exploited the Kuwajima alkylation protocol.[15] Treatment of the enol silyl ether derived from **10** (LDA/Me_3SiCl) with allyl bromide and BTAF afforded a 1:1 epimeric mixture of monoalkylated ketones which, on base-catalyzed equilibration, led to the more stable equatorial isomer **11** (≥98:1); the yield from **10** was 59%.

The second major difficulty concerned the actual generation of the furan ring system. In particular, the cyclization–dehydration of keto aldehyde **12**, obtained from **11** by ozonolysis followed by reductive workup (triphenylphosphine), proved less than straightforward. Fortunately, after considerable experimentation (+)-pallescensin A (**8**) was obtained via treatment of **12** with $BF_3{\cdot}Et_2O$ in benzene with azeotropic removal of water (Dean–Stark). The yield ranged from 30–40%. That in fact (+)-pallescensen A (**8**) was in hand derived from careful spectral comparison (^1H NMR and IR) with authentic spectra kindly provided by Dr. T. Oishi of the Institute of Physical and Chemical Research (Riken)[18] and Professor S. Tanis, Michigan State University.[18] The optical rotation $[\alpha]^{24}_D$ was +81.3° ($CHCl_3$, *c* 1.3); lit.[17b] $[\alpha]^{22}_D$ +60.4° ($CHCl_3$, *c* 0.9).[19]

In summary, we have developed an efficient, synthetic route to chiral, nonracemic *trans*-decalone derivatives from readily available (+)-Wieland–Miescher ketone. To demonstrate the utility of this strategy, we have completed a nine-step, enantioselective synthesis of (+)-pallescensin A (**8**).

Experimental Section

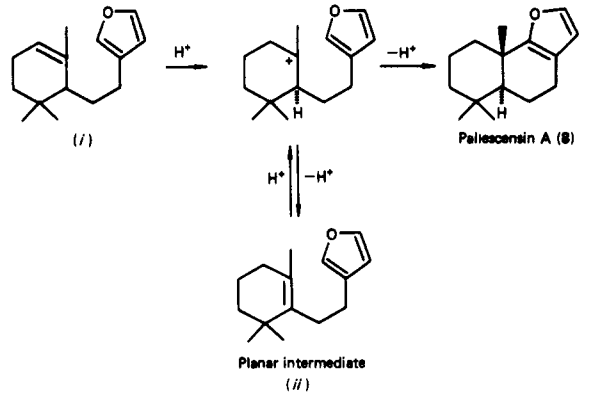
Materials and Equipment. Melting points were obtained on a Thomas-Hoover instrument and are corrected. All solvents used were reagent grade. Ether and THF were distilled from sodium and benzophenone. Precoated silica gel plates (250 μm) with a fluorescent indicator (Merck) were used for analytical thin-layer chromatography (TLC). Visualization was achieved via ultraviolet light or ethanolic molybdophosphoric acid [7% (w/v)]. Silica gel 60 (particle size 0.043–0.063 mm) supplied by Merck was used for flash chromatography. Proton NMR spectra were obtained for deuteriochloroform solutions on either a Varian T-60A (60 MHz) or a Bruker WP-250 FT (250 MHz) spectrometer. Chemical shifts are reported in δ values relative to tetramethylsilane. All infrared spectra were recorded on either a Perkin-Elmer Model 337 or Model 283B spectrophotometer. Optical rotations were obtained on a Perkin-Elmer Model 241 polarimeter. High-resolution mass spectra were obtained from the University of Pennsylvania Mass Spectrometry Service Center on a Hitachi Perkin-Elmer RMH-2 or VG 70-70 Micromass double-focusing spectrometer interfaced with a Kratos DS-50-S data system.

Preparation of (+)-Phenylthio Enone 4. A solution of (+)-5,5-(ethylenedioxy)-10-methyl-$\Delta^{1(9)}$-octalin-2-one (**6**)[13] (2.65 g, 11.9 mmol), freshly distilled thiophenol (17.9 mmol, 1.5 equiv), 37% aqueous formaldehyde (19.4 mmol, 1.63 equiv), triethylamine (15 mmol, 1.26 equiv), and ethanol (10 mL) was heated to reflux under nitrogen for 4 days. The solution was cooled and partitioned between 5% potassium hydroxide (50 mL) and ether (100 mL). The organic layer was washed with 5% potassium hydroxide (25 mL), and the combined aqueous layers were washed with ether (100 mL). The organic layers were combined and washed with brine and dried over anhydrous magnesium sulfate. Evaporation

(17) (a) Matsumoto, T.; Usui, S. *Chem. Lett.* 1978, 105. (b) Akita, H.; Oishi, T. *Chem. Pharm. Bull.* **1981**, *29*, 1580.

(18) We thank Dr. T. Oishi and Professor S. Tanis, respectively, for providing authentic spectra and an authentic racemic sample of pallescensin A (**8**).

(19) The optical rotation reported by Matsumoto and co-workers,[17a] $[\alpha]$ +26.4 ($CHCl_3$), is considerably lower than either that obtained by Oishi[17b] or from this work. Assuming high enantiomeric purity of the Matsumoto starting olefin (**i**), the low rotation and thereby enantiomeric purity of pallescensin A (**8**) may be explicable in terms of the planar intermediate (**ii**).



(20) Snitman, D. L.; Tsai, M.-Y.; Watt, D. S.; Edwards, C. L.; Stotter, P. L. *J. Org. Chem.* **1979**, *44*, 2838.

of the solvent afforded a crystalline product which was washed with cold ether (10–20 mL). The washings were concentrated and chromatographed (20% ethyl acetate–hexane) to yield a total of 3.58 g (87%) of **4**: mp 89–91 °C (ether); $[\alpha]^{28}_D$ +147.4° (*c* 1.0, benzene); IR (CCl_4) 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (3 H, s, CH_3), 1.45–2.70 (10 H, m), 3.75 (1 H, d, *J* = 11.6 Hz), 3.85–4.00 (5 H, m), 7.22–7.40 (5 H, m, Ar H); mass spectrum, *m/e* 344.1442 (M^+ calcd for $C_{20}H_{24}O_3S$, 344.1446).

Anal. Calcd for $C_{20}H_{24}O_3S$: C, 69.73; H, 6.97. Found: C, 69.66; H, 6.99.

General Procedure for Reductive Alkylation of 4. Typically, a solution of enone **4** (10 mmol), water (2 equiv), and tetrahydrofuran (20 mL) was added to a stirred solution of 3 equiv of lithium in liquid ammonia (300 mL) over a 20–30-min period. The solution was allowed to stir for another 45 min, whereupon 80 mL of tetrahydrofuran was added followed by rapid addition of the alkylating agent (15 equiv) dissolved in tetrahydrofuran (20 mL). The reaction was allowed to stir for 30 min after which the ammonia was allowed to evaporate. The residue was diluted with ether and extracted with water. The organic layer was then washed with brine, dried over anhydrous magnesium sulfate, and concentrated to yield a yellow oily residue, which was chromatographed (5% ethyl acetate–hexane) to yield the respective ketone.

1a–Methyl iodide: mp 69.5–70.0 °C (hexane); $[\alpha]^{24}_D$ −34.8° (*c* 1.8, $CHCl_3$); IR ($CDCl_3$) 1690 cm^{-1}; ^1H NMR ($CDCl_3$) 1.05 (3 H, s, CH_3), 1.08 (3 H, s, CH_3), 1.25 (3 H, s, CH_3), 3.82–4.00 (4 H, m, OCH_2CH_2O).

1b[3b]–Allyl bromide: $[\alpha]^{25}_D$ +26.8° (*c* 1.4, $CHCl_3$); IR (CCl_4) 3065, 1635, 910 (terminal olefin), and 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (3 H, s, CH_3), 1.21 (3 H, s, CH_3), 1.32–2.63 (13 H, complex), 3.80–3.96 (4 H, m, OCH_2CH_2O), 4.94–5.04 (2 H, m, $CH_2CH{=}CH_2$), 5.58–5.74 (1 H, m, $CH_2CH{=}CH_2$); mass spectrum, *m/e* 278.1895 (M^+ calcd for $C_{17}H_{26}O_3$, 278.1882).

1c–Benzyl bromide: mp 83.5–84.5 °C (hexane); $[\alpha]^{25}_D$ +21.2° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) 3635, 1695; ^1H NMR ($CDCl_3$) δ 1.10 (3 H, s, CH_3), 1.12 (3 H, s, CH_3), 1.15–1.75 (8 H, complex), 2.15–2.50 (3 H, complex), 2.55 (1 H, d, *J* = 13.4 Hz), 3.14 (1 H, d, 13.4 Hz), 3.72–3.92 (4 H, m, OCH_2CH_2O), 7.03–7.29 (5 H, m, Ar H); mass spectrum, *m/e* 238.2048 (M^+ calcd for $C_{21}H_{28}O_3$, 328.2038).

Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.85; H, 8.53. Found: C, 77.00; H, 8.55.

1d–Cinnamyl bromide: mp 101–102 °C (ether); $[\alpha]^{22}_D$ +7.4° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$) 3010, 2950, 2890, 1702, 1605, 1605, 1445, 1385, 1190 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (3 H, s), 1.21 (3 H, s), 1.32–2.75 (13 H, complex), 3.81–3.93 (4 H, m), 6.04–6.14 (1 H, m), 6.35 (1 H, d, *J* = 15.9 Hz), 7.16–7.35 (5 H, m); mass spectrum, *m/e* 354.2201 (M^+ calcd for $C_{23}H_{30}O_3$, 354.2195).

Anal. Calcd for $C_{23}H_{30}O_3$: C, 77.98; H, 8.47. Found: C, 77.90; H, 8.56.

1e–*n*-Butyl iodide: $[\alpha]^{25}_D$ +2.1° (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (3 H, t, *J* = 7.1 Hz), 1.01 (3 H, s, CH_3), 1.17 (3 H, s, CH_3) 1.00–1.75 (16 H, complex), 1.80–2.16 (2 H, m), 2.80–2.56 (2 H, m), 3.90 (4 H, m, OCH_2CH_2O); mass spectrum, *m/e* 294.2193, (M^+ calcd for $C_{18}H_{30}O_3$, 294.2195).

Anal. Calcd for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27. Found: C, 73.50; H, 10.25.

1g–*trans*-3-Pentenyl iodide.

Trimethylsilyl Enol Ether 7.[20] A solution of **4** (255 mg, 0.74 mmol) in THF (4 mL) containing *tert*-butyl alcohol (102 mg, 1.38 mmol) was added dropwise over 10 min to a solution of lithium (30.8 mg, 4.4 mmol) in ammonia (25 mL). The solution was stirred for 15 min, and the excess lithium was destroyed by addition of a few drops of isoprene. The ammonia was evaporated under a stream of argon at 0 °C and finally at room temperature (1 h). THF (5 mL) was then added and the reaction was cooled to 0 °C followed by the rapid addition of a quenching solution of chlorotrimethylsilane (4.4 mmol) and triethylamine (4.4 mmol) in 3 mL of THF (previously centrifuged to remove ammonium salt). The reaction was stirred for 15 min and poured into an ether–cold saturated aqueous sodium bicarbonate mixture. The organic layer was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded 230 mg (100%) of **7** as a yellow oil. NMR analysis indicated a single compound which was used without further purification: IR ($CHCl_3$) 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.16 (s, 9 H), 0.93 (s, 3 H), 1.51 (br s, 3 H), 1.10–2.42 (11 H, complex), 3.92 (m, 4 H).

Formylation of Enone 4. To a lithium ammonia solution (4.4 mmol of lithium in 25 mL of ammonia) was slowly added a solution of enone **4** (0.73 mmol) in tetrahydrofuran (3 mL) containing water (1.44 mmol). The solution was allowed to stir for 10 min, whereupon the excess lithium was destroyed by the addition of isoprene. The ammonia was allowed to evaporate under a flow of argon over a 2-h period. Tetrahydrofuran was added (3 mL), and the reaction was cooled to −78 °C, followed by the addition of gaseous formaldehyde which was bubbled through the solution for 3 min. The reaction was then poured into ether (8 mL) and water (40 mL). The aqueous layer was washed with ether (80 mL) and the combined organic material was washed with brine, dried over anhydrous magnesium sulfate, and concentrated. Flash chromatography (1:2, ethyl acetate–hexane) gave 82 mg (42%) of **1f**.[5b,c]

Keto Alcohol 1f.[5b,c] To a solution of silyl enol ether **7** (110 mg, 0.36 mmol) in tetrahydrofuran (4 mL) was added methyllithium (1 equiv) at 0 °C. After 15 min the solution was cooled to −45 °C (acetonitrile–dry ice bath) and formaldehyde was bubbled through the solution for 10 min. The solution was then diluted with ether (50 mL) and water (20 mL). The organic layer was washed with brine, dried with anhydrous magnesium sulfate, concentrated, and chromatographed (33% ethyl acetate–hexane) to yield 59 mg (62%) of **1f**: $[\alpha]^{24}_D$ −67.9° (*c* 1.4, $CHCl_3$); IR ($CHCl_3$) 3610, 3000, 2960, 2790, 1692, 1055, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (3 H, s), 1.28 (3 H, s), 1.32–2.72 (12 H, complex), 3.40 (1 H, dd, *J* = 11.4, 6.8 Hz), 3.60 (1 H, dd, *J* = 11.4, 6.8 Hz), 3.37–3.96 (4 H, m); mass spectrum, *m/e* 268.1747 (M^+ calcd for $C_{15}H_{24}O_4$, 268.1752).

1,1-(Ethylenedioxy)-5,5,9-trimethyl-*trans*-decalin (9).[20] A solution of **1a** (555 mg, 2.33 mmol) and hydrazine (2.9 mL) in triethylene glycol (10 mL) was heated at 125 °C under an argon atmosphere for 2 h after which potassium hydroxide (0.82 g) was added. The excess hydrazine was removed by distillation and the reaction was heated at 190 °C for 10 h. The solution was cooled, diluted with ether, washed with water and brine, and dried over anhydrous magnesium sulfate. The solvent was removed in vacuo and the resultant oil quickly filtered through silica gel by using 1:10 ethyl acetate–hexane to afford 514 mg (93%) of **9**: $[\alpha]^{24}_D$ −18.9° (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) 2940, 1460, 1230, 1200, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82 (s, 3 H), 0.86 (s, 3 H), 1.05 (s, 3 H), 1.15–1.75 (13H, complex), 3.90 (m, 4 H); mass spectrum *m/e* 238.1937, (M^+ calcd for $C_{15}H_{26}O_2$, 238.1932).

5,5,9-Trimethyl-*trans*-1-decalone (10).[20] A solution of **9** (461 mg, 1.94 mmol) in THF (10 mL) containing 3 N hydrochloric acid (5 mL) was allowed to stir for 2 h. The solution was diluted with ether and washed successively with water, saturated aqueous sodium bicarbonate, and brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated in vacuo and the crude product chromatographed (silica gel; 10% ethyl acetate–hexane) to yield 367 mg (98%) of **10**: $[\alpha]^{24}_D$ −42.3° (*c* 2.4, $CHCl_3$); IR ($CHCl_3$) 2945, 1695, 1455, 1385, 1375, 1365 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (s, 3 H), 0.92 (s, 3 H), 1.14 (s, 3 H), 1.30–2.50 (12 H, complex), 3.90 (4 H, m); mass spectrum, *m/e* 194.1674 (M^+ calcd for $C_{13}H_{22}O$, 194.1671).

2-Allyl-5,5,9-trimethyl-*trans*-1-decalone (11). A solution of decalone **10** (388, 2.0 mmol) in THF (2 mL) was added dropwise to a solution of lithium diisopropylamide (1.2 equiv) in THF (6 mL) at 0 °C. The solution was allowed to stir for 15 min, whereupon a solution of chlorotrimethylsilane (0.61 mL) and triethylamine (0.67 mL) in THF (3 mL) was added. The reaction was stirred for 15 min, diluted with hexane (60 mL), and poured into cold saturated aqueous sodium bicarbonate. The organic layer was washed with brine and dried over anhydrous sodium bisulfate. The solvent was evaporated in vacuo and the crude product dissolved in dry benzene (50 mL), and the solvent was evaporated once again to afford 530 mg (100%) of the corresponding silyl enol ether: IR ($CHCl_3$) 2955, 1654, 1454, 1349, 885, 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.17 (9 H, s), 0.84 (3 H, s), 0.88 (3 H, s), 1.05 (3 H, s), 1.07–2.06 (11 H, complex), 4.53 (1 H, t, *J* = 3.5 Hz).

Without purification the silyl enol ether (1.9 mmol) was dissolved in THF (2 mL) containing allyl bromide (0.5 mL, 5 equiv) and added to a suspension of benzyltrimethylammonium fluoride

(BTAF) (482 mg, 1.5 equiv) in THF (4 mL) containing 4-Å molecular sieves (0.5 g). The reaction was allowed to stir for 3 h. Filtration and removal of the solvent in vacuo followed by chromatography (silica gel, 5% ethyl acetate–hexane) afforded 275 mg (61.9%) of product whose NMR analysis indicated it to be a 1:1 mixture of epimers. This mixture was dissolved in methanol (25 mL) containing potassium bicarbonate (0.7g) and allowed to stir for 3 h. The solvent was evaporated, followed by dissolving the resultant product in methylene chloride. After a quick filtration through Florisil, the solvent was again removed in vacuo to afford 261 mg (58.7%) of 11: $[\alpha]^{24}_D$–20° (c 1.4, $CHCl_3$); IR ($CHCl_3$) 2940, 1699, 16408 1460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (3 H, s), 0.92 (3 H, s), 1.13 (3 H, s), 1.20–2.68 (14 H, complex), 4.95–5.03 (2 H, m), 5.71–5.86 (1 H, m); mass spectrum, *m/e* 234.1982 (M^+ calcd for $C_{16}H_{26}O$, 234.1984).

Anal. Calcd for $C_{16}H_{26}O$: C, 82.05; H, 11.10. Found: C, 82.10; H, 11.10.

Keto Aldehyde 12. Ozone was passed through a solution of **11** (62 mg, 0.27 mmol) in methylene chloride (25 mL) for 15 min at −78 °C. Triphenylphosphine (0.4 mmol) was then added to the solution as it was allowed to warm to room temperature. After 2 h the solvent was evaporated and the resultant material chromatographed (silica gel, 10% ethyl acetate–hexane) to yield 54 mg (85%) of **12**: $[\alpha]^{25}_D$ −19° (c 1.2, $CHCl_3$); IR ($CHCl_3$) 2735, 1725, 1705, 1463, 1390, 1380, 1362, 995 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (3 H, s), 0.92 (3 H, s), 1.19 (3 H, s), 1.06–2.22 (12 H, complex), 2.88 (1 H, dd, J = 17, 7 Hz), 3.27 (1 H, m), 9.79 (1 H, br s); mass spectrum, *m/e* 237.1841 (M^+ calcd for $C_{15}H_{25}O_2$, 237.1858).

(+)-Pallescensin A (8). Keto aldehyde **12** (17 mg, 0.07 mmol) was added to a solution of dry benzene (30 mL) containing 2 drops of boron trifluoride–etherate. The solution was heated to reflux for 1 h with water removal (Dean–Stark apparatus). The solution was allowed to cool and then diluted with ether (50 mL) and water (40 mL). The organic layer was washed with brine, dried over anhydrous magnesium sulfate, concentrated in vacuo, and chromatographed (silica gel, hexanes) to afford 5.6 mg (35%) of **8**, the spectroscopic data (NMR and IR) of which were identical with those of authentic spectra of natural pallescensin A (**8**):[17b] $[\alpha]^{25}_D$ +81.3° (c 1.3, $CHCl_3$); IR ($CHCl_3$) 2930, 2858, 1500, 1460, 1375 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.92 (6 H, s), 1.18 (3 H, s), 1.20–2.70 (11 H, complex), 6.08 (1 H, d, J = 2 Hz), 7.15 (1 H, d, J = 2 Hz); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.91 (3 H, s), 0.93 (3 H, s) 1.19 (3 H, s), 1.21–1.90 (8 H, complex), 2.08–2.16 (1 H, m), 2.30–2.57 (2 H, m), 6.11 (1 H, d, J = 1.8 Hz), 7.18 (1 H, d, J = 1.8 Hz).

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Enantioselectivity of Microbial Hydrolysis of (±)-Decahydro-2-naphthyl Acetates. Preparations and Absolute Configurations of Chiral Decahydro-2-naphthols

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Absolute configurations of chiral decahydro-2-naphthols, which were obtained by microbial hydrolysis of corresponding (±)-acetates and chloroacetates, were elucidated by chemical correlation to (4a*S*,8a*S*)-*trans*-octahydro-2(1*H*)-naphthalenone (**5**). Decarboxylation of the (−)-α-methylbenzylamine salt of (−)-2-oxo-2,3,4,4a,5,6,7,8-octahydro-4a-naphthalenecarboxylic acid (**1a**) gave (+)-(*S*)-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (**3**), which was reduced with lithium in liquid ammonia to (+)-(4a*S*,8a*S*)-*trans*-octahydro-2-(1*H*)-naphthalenone (**5**). Catalytic hydrogenation of (−)-**3** gave (−)-(4a*R*,8a*S*)-*cis*-octahydro-2(1*H*)-naphthalenone (**4**), which was already obtained by oxidation of (−)-*cis*,*cis*-decahydro-2-naphthol (**7**) with chromic acid. These results mean that (−)-**7** has the 2*S*,4a*R*,8a*S* configuration. Furthermore, the absolute configuration of (−)-**7** was confirmed by X-ray analysis of its *p*-bromobenzoate.

(±)-Monocyclic monoterpene alcohols can be effectively resolved by microbial hydrolysis of corresponding acetates[1] and chlforoacetates.[2] In order to extend this enzymic resolution to (±)-bicyclic sesquiterpene alcohols, it is necessary to elucidate the stereochemistry on the microbial hydrolysis of (±)-decahydro-1- and 2-naphthyl acetates[2,3] having their fundamental ring structure. Already, chiral decahydronaphthols having an (*S*)-hydroxyl group had been prepared by microbial reduction of (±)-octahydronaphthalenones by Prelog et al.[4] But the reduction of (±)-*cis*-octahydro-2(1*H*)-naphthalenone (**4**) gave only racemic decahydro-2-naphthols, cis,cis form[5] **7**, and cis,trans

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(4) Prelog, V.; Smith, H. E. *Helv. Chim. Acta* **1959**, *42*, 2624.
(5) First cis for C-4a and C-8a hydrogens, second cis for C-2 and C-8a hydrogens on decahydro-2-naphthols, see: "Dictionary of Organic Compounds", 5th ed.; Chapman and Hall: London, 1982.

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