

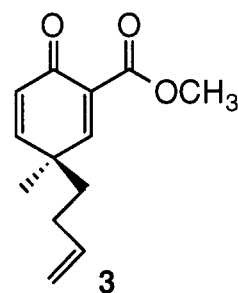
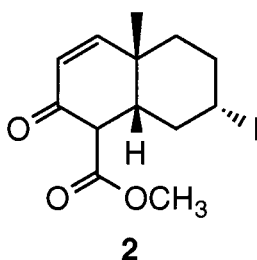
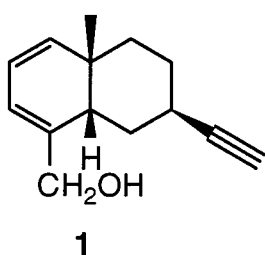
A FORMAL SYNTHESIS OF (-)-DEHYDROCHAMAECYNENOL.
ASYMMETRIC SYNTHESIS OF AN ADVANCED KEY INTERMEDIATE¹

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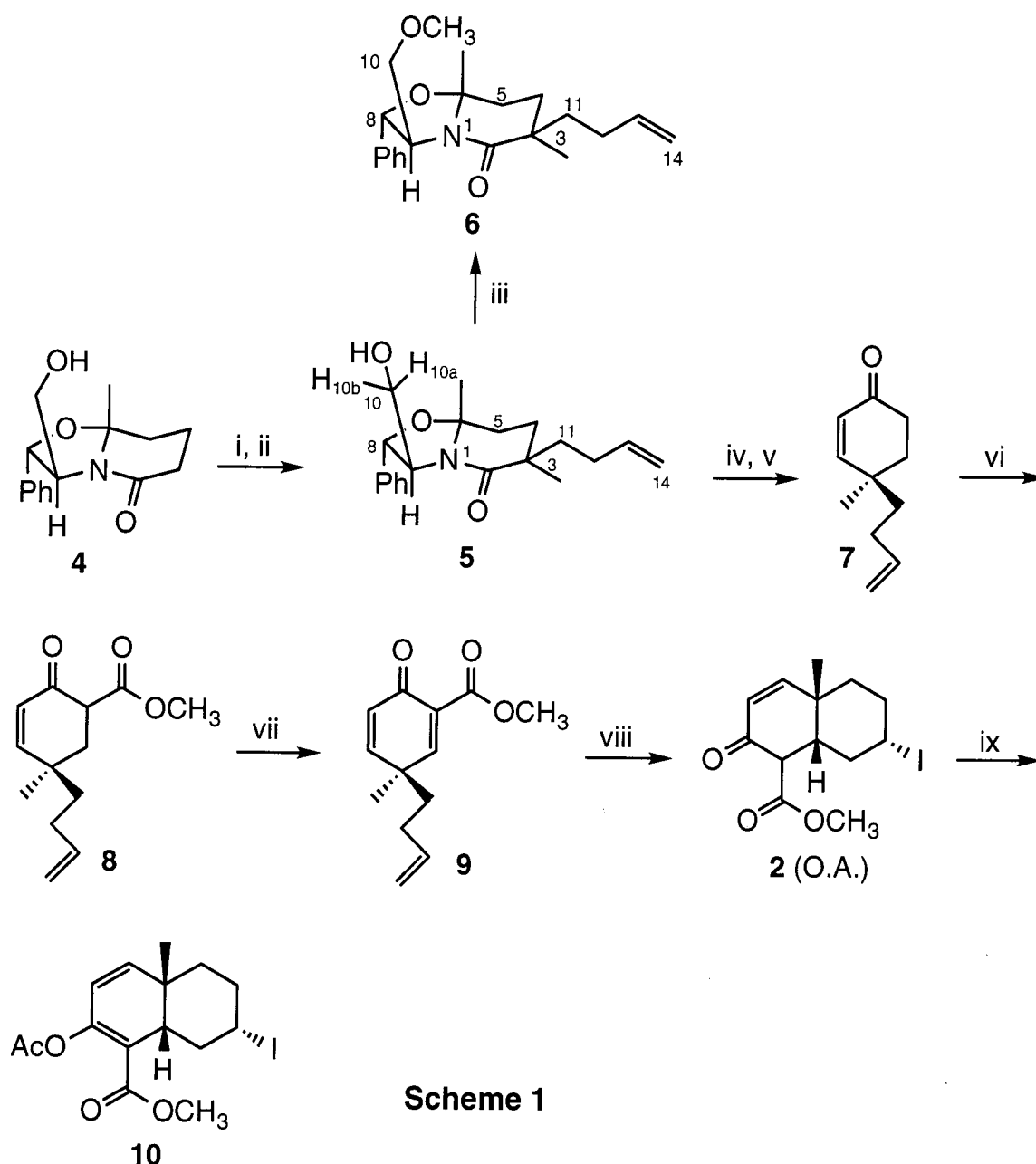
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Abstract – Keto ester (**2**), which served as an advanced intermediate in the total synthesis of ($\pm$)-dehydrochamaecynenol (**1**), has been prepared in optically active form.

(-)-Dehydrochamaecynenol (**1**), a highly unsaturated norsesquiterpene, was first isolated from *Chamaecyparis formosensis* Matsum three decades ago by Nozoe and co-workers.³ Recently, we reported the first total synthesis, in racemic form, of this structurally interesting natural acetylene⁴ *via* the intermediacy of keto ester (**2**). This key intermediate was readily prepared from compound (**3**) by a facile polyene cyclization reaction promoted by the cross conjugated α -carbomethoxy enone system. Herein, we wish to report the synthesis of nonracemic keto ester (**2**). In addition to serving as a synthesis precursor leading to dehydrochamaecynenol in natural form based on the developed route for its racemic modification,⁴ this chiral compound may find extensive use as an advanced intermediate for the construction of a variety of naturally occurring compounds, especially those of the cadinane family.



Following the general procedure of Meyers *et al.*,⁵ the commercially available (+)-lactam (**4**) of known absolute configuration was subjected to sequential alkylation with 4-bromo-1-butene and methyl iodide using lithium diisopropylamide as a base (Scheme 1). The desired epimer (**5**) was produced virtually exclusively in 50% yield over two steps.



(i) LDA, 4-bromo-1-butene, THF, 0 °C, 24 h, 91%; (ii) LDA, CH₃I, THF-DMPU, -78 °C, 6 h, 54%; (iii) NaH, CH₃I, THF, rt, 24 h, 95%; (iv) Red-Al, C₆H₅CH₃, rt, 12 h; (v) *n*-Bu₄NH₄⁺H₂PO₄⁻, H₂O, C₂H₅OH, reflux, 24 h, 65% over two steps; (vi) NaH, (CH₃O)₂CO, reflux, 1 h, 91%; (vii) DDQ, C₆H₆, reflux, 5 h, 87%; (viii) ZnI₂, ether, rt, 3 days, 82% ; (ix) Ac₂O, Py, rt, overnight, 93%.

Attempts to confirm its stereochemistry, which was tentatively assigned previously,⁶ by NOE experiments were inconclusive (Figure 1) due to complications caused most likely by the intramolecular hydrogen bonding between the hydroxyl group and the lactam carbonyl. This problem was circumvented by formation of the corresponding methyl ether (**6**) using sodium hydride and methyl iodide. The stereochemistry of this compound could be unambiguously deduced on the basis of the NOE experimental results (Figure 2). This simple structural modification promises to have general utility in rapid verification of the stereochemistry of derivatives of **4** and related compounds, which has been typically carried out by X-Ray analysis. Removal of the chiral auxiliary was effected by reduction of the amido group to carbinol amine with Red-Al in toluene followed by treatment with aqueous tetrabutylammonium dihydrogen phosphate.⁵ The latter reagent induced an array of ring cleavage as well as the aldol condensation of the resulting keto aldehyde to give (*R*)-enone (**7**) ($[\alpha] = +75.0^\circ$) in 64% overall yield. Enone (**7**) was subjected to carbomethoxylation using dimethyl carbonate and sodium hydride to give keto ester (**8**) (91% yield) as a mixture of three rapidly interconvertible components: a pair of diastereomers and the corresponding enol form in a ratio of 1:1:3 as indicated by the ^1H NMR spectrum. Subsequent oxidation of keto ester (**8**) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) resulted in the formation, in 87% yield, of (*S*)-enone ester (**9**), $[\alpha] = +27.8^\circ$. The cyclization of this compound was effected by zinc iodide in ether, and after three days at room temperature, the optically active bicyclic iodide (**2** (O.A.)), existing as a mixture of epimers (30%) and the enol tautomer (70%) due to the labile center flanked by two carbonyl groups, was produced in 82% yield. The identity of this compound was fully established by direct comparison with the corresponding racemic modification prepared previously in our laboratory⁴ and by acetylation with acetic anhydride and pyridine. Enone acetate (**10**) thus obtained in 93% yield displayed NOE results (Figure 3) in complete agreement with the depicted stereochemistry.

Since the racemic keto ester (**2**) has been transformed previously, in eight steps, into ($\pm$)-dehydrochamaecynenol (**1**), the preparation of the nonracemic version (**2** (O.A.)) possessing the same absolute configuration as that found in the naturally occurring levorotatory compound

constitutes a formal synthesis of the natural material. In addition, chiral keto ester (**2** (O.A.)) may prove to be a highly useful synthetic precursor for a variety of other natural compounds.

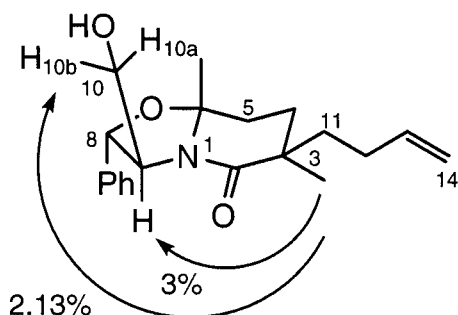


Figure 1. NOE data of compound **5**

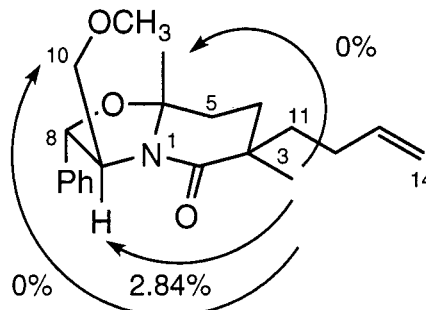


Figure 2. NOE data of compound **6**

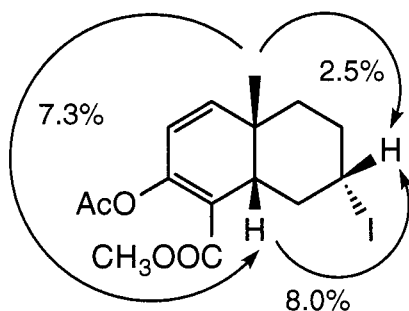


Figure 3. NOE data of compound **10**

EXPERIMENTAL

General and Material

Solvents used were distilled from appropriate drying agents. Melting points are not corrected. Combustion elemental analyses were performed by the microanalytical laboratory of this department. Fourier transform infrared spectra were recorded on a Nicolet 7199 or Nicolet MX-1 FTIR spectrophotometer. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on a Bruker WH-200, Bruker WH-300 spectrometer using deuteriochloroform (CDCl_3) as solvent unless otherwise stated. Tetramethylsilane (TMS) was used as an internal reference. Coupling constants are reported to ± 0.5 Hz. Chemical shift measurements are reported in ppm downfield from TMS in delta (δ) units. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broad. Carbon-13 nuclear

magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker WH-300 (75 MHz) spectrometer, and were obtained as solutions in deuteriochloroform as the internal standard setting the central peak at 77.00 ppm. Methyl and methine groups are shown as signals possessing an antiphase (a) with respect to the deuteriochloroform signal, whereas methylene groups, quaternary carbons and carbonyl groups appear in phase (p) with it. Nuclear Overhauser Enhancement (NOE) experiments were determined in the difference mode in which a control (undecoupled) spectrum was computer subtracted from the irradiated spectrum after Fourier transformation. Positive enhancements are defined as signals possessing an antiphase with respect to the irradiated signal. Samples for NOE measurements were deoxygenated with argon for 10 min prior to use. High resolution electron impact mass spectra (HRMS) were recorded using an A.E.I. model MS-50 mass spectrometer. Optical rotations were determined on a Perkin Elmer 241 polarimeter with sodium (589 nm) lamp.

(3S, 6R, 8S, 9R)-1-Aza-3-(3-butenyl)-9-hydroxymethyl-3,6-dimethyl-8-phenyl-7-oxabicyclo[4.3.0]nonan-2-one (5)

To a stirred solution of diisopropylamine (3.3 mL, 25.2 mmol) in dry THF (25 mL) under argon at 0 °C, was added dropwise *n*-BuLi (8.8 mL, 2.5 M in hexane, 22 mmol). After being stirred for 20 min at 0 °C, the solution was cooled to -78 °C. A solution of lactam (**4**) (2 g, 7.8 mmol) in THF (5 mL) was added *via* syringe. The solution was immediately warmed to 0 °C, stirred for 2 h and then cooled again to -78 °C. 4-Bromo-1-butene (2.4 mL, 24.2 mmol) was added. After being stirred for 15 min at -78 °C, the solution was warmed to 0 °C and stirred at this temperature overnight. The reaction was quenched with 1 N HCl (20 mL) and the resulting mixture concentrated *in vacuo* to remove THF. The acidic aqueous layer was extracted with dichloromethane, and the combined organic solutions were then washed with brine, dried over MgSO_4 , filtered and concentrated *in vacuo* to give a yellow oil which was subjected to flash chromatography. Elution with ethyl acetate/hexane (60:40) gave a mixture of two diastereomeric monoalkylated lactams (1.1 g, 91% yield based on the consumed starting material), which was used directly for the subsequent transformation. Further elution with the same solvent system gave the starting material (1 g).

To a stirred solution of diisopropylamine (1.7 mL, 12 mmol) in dry THF (20 mL) under argon at 0 °C, was added *n*-BuLi (4.4 mL, 2.5 M in hexane, 11 mmol). After being stirred at 0 °C for 15 min, DMPU (10 mL) was added. The solution was cooled to -78 °C, and a solution of the above monoalkylated lactams (1.1 g, 4 mmol) in THF (4 mL) was added. The reaction mixture was warmed to 0 °C, stirred for 3 h and then cooled to -78 °C. Iodomethane (0.75 mL, 12 mmol) was added. After being stirred for 20 min, the reaction mixture was warmed to rt, and stirred overnight. The reaction was quenched with 1 N HCl, and the resulting mixture concentrated *in vacuo* to remove THF. The aqueous layer was extracted with ether. The combined organic solutions were washed with water and brine, dried over MgSO₄, filtered and concentrated *in vacuo* to give a yellow liquid. Flash chromatography of the liquid with ethyl acetate/hexane (50:50) gave lactam (**5**) as a white solid and then the starting material (200 mg). Recrystallization from ethyl acetate/hexane gave pure lactam (**5**) (0.5 g, 54% based on the consumed starting material): mp 169-171 °C; [α]_D²⁰ = -9.5° (c 1.55, EtOH); IR (uscope) 3439 (OH) and 1641 (C=O) cm⁻¹; ¹H NMR (300 MHz) δ 7.42-7.25 (m, 5H, aromatic H), 5.85 (dddd, J = 17, 10, 6.5, 6.5 Hz, 1H, CH=CH₂), 5.07 (dddd, J = 17, 1.5, 1.5, 1.5 Hz, 1H, *trans* CH=CHH), 4.98 (dddd, J = 10, 1.5, 1.5, 1.5 Hz, 1H, *cis* CH=CHH), 4.81 (d, J = 8.5 Hz, 1H, H₈), 4.39 (br s, 1H, OH), 4.11 (ddd, J = 8.5, 8.5, 2.5 Hz, 1H, H₉), 3.92 (dd, J = 11, 2.5 Hz, 1H, H_{10a}), 3.76 (dd, J = 11, 8.5 Hz, 1H, H_{10b}), 1.45-2.30 (m, 8H), 1.60 (s, 3H, C₆-CH₃), 1.25 (s, 3H, C₃-CH₃); ¹³C NMR (75 MHz) δ 176.3 (p), 138.1 (a), 137.9 (p), 128.9 (a), 128.8 (a, 2 x C), 126.7 (a, 2 x C), 114.9 (p), 94.0 (p), 78.6 (a), 67.1 (a), 65.4 (p), 41.7 (p), 39.6 (p), 32.7 (p), 29.5 (p), 28.9 (p), 26.5 (a), 24.5 (a); HRMS M⁺ 329.1995 (calcd for C₂₀H₂₇NO₃: 329.1991). Anal. Calcd for C₂₀H₂₇NO₃: C 72.92, H 8.26. Found: C 72.52, H 8.63.

(3*S*, 6*R*, 8*S*, 9*R*)-1-Aza-3-(3-butenyl)-9-methoxymethyl-3,6-dimethyl-8-phenyl-7-oxabicyclo[4.3.0]nonan-2-one (**6**)

To a stirred suspension of the bicyclic lactam (**5**) (165 mg, 0.5 mmol) in THF (10 mL) at 0 °C under argon, were added NaH (25 mg, 95%, 1 mmol) and iodomethane (0.063 mL, 1 mmol). The reaction mixture was allowed to warm to ambient temperature and stirred overnight. The reaction was then quenched with saturated NH₄Cl. The aqueous solution was extracted with

ether (3 x 30 mL). The combined organic solutions were washed with water and brine, dried over MgSO_4 , filtered and concentrated. The crude product was purified by flash chromatography using ethyl acetate/hexane (10:90) as an eluent to afford lactam (**6**) (163 mg, 95%) as a white solid: mp 83-84 °C (*n*-hexane-ethyl acetate); $[\alpha]_{\text{D}}^{20} = -10.0^\circ$ (c 0.76, EtOH); IR (CH_2Cl_2) 1641 (C=O) cm^{-1} ; ^1H NMR (300 MHz) δ 7.42-7.25 (m, 5H, aromatic H), 5.82 (dddd, $J = 17, 10, 6.5, 6.5$ Hz, 1H, $\text{CH}=\text{CH}_2$), 5.25 (d, $J = 8.5$ Hz, 1H, H_8), 5.04 (dddd, $J = 17, 1.5, 1.5, 1.5$ Hz, 1H, *trans* $\text{CH}=\text{CHH}$), 4.96 (dddd, $J = 10, 1.5, 1.5, 1.5$ Hz, 1H, *cis* $\text{CH}=\text{CHH}$), 4.11 (ddd, $J = 8.5, 4.5, 3$ Hz, 1H, H_9), 3.74 (dd, $J = 10, 4.5$ Hz, 1H, H_{10a}), 3.65 (dd, $J = 10, 3$ Hz, 1H, H_{10b}), 3.48 (s, 3H, OCH_3), 1.45-2.30 (m, 8H), 1.61 (s, 3H, $\text{C}_6\text{-CH}_3$), 1.27 (s, 3H, $\text{C}_3\text{-CH}_3$); ^{13}C NMR (75 MHz) δ 174.3 (p), 139.4 (p), 138.4 (a), 128.6 (a), 128.3 (a, 2 x C), 126.7 (a, 2 x C), 114.7 (p), 93.7 (p), 78.8 (a), 71.0 (a), 63.3 (p), 59.3 (a), 41.9 (p), 40.1 (p), 33.0 (p), 29.6 (a), 28.9 (p), 26.4 (a), 24.2 (a); HRMS M^+ 343.2156 (calcd for $\text{C}_{21}\text{H}_{29}\text{NO}_3$: 343.2148). Anal. Calcd for $\text{C}_{21}\text{H}_{29}\text{NO}_3$: C 73.44, H 8.51. Found: C 73.68, H 8.26.

(R)-4-(3-Butenyl)-4-methyl-2-cyclohexenone (**7**)

To a stirred solution of the dialkylated lactam (**5**) (1.3 g, 3.95 mmol) in dry toluene (20 mL) at -78 °C under argon, was added a 3.4 M solution of Red-Al in toluene (2.87 mL, 9.76 mmol). The reaction mixture was allowed to warm to rt and stirred for 12 h. Methanol was cautiously added with stirring to destroy excess Red-Al. The resulting solution was extracted with ether (3 x 100 mL). The combined organic solutions were washed with water and brine, dried over MgSO_4 , filtered and evaporated to dryness. The residue was dissolved in ethanol (25 mL). A 1 M aqueous solution of tetra-*n*-butylammonium dihydrogen phosphate (15 mL) was added, and the resulting mixture was heated under reflux with stirring for 24 h. The solution was cooled and concentrated to remove most of the ethanol. The residue was extracted with ether (3 x 100 mL). The combined extracts were washed with water and brine, dried over MgSO_4 , filtered and evaporated to dryness. The crude product was subjected to flash chromatography using ethyl acetate/hexane (5:95) as an eluent to give (+)-**7** (0.42 g, 65%) as a colorless oil: $[\alpha]_{\text{D}}^{20} = +75.7^\circ$ (c 1.50, EtOH); IR (CH_2Cl_2 cast) 1684 (C=O, enone) and 1646 (C=C) cm^{-1} ; ^1H NMR (200 MHz) δ 6.70 (d, $J = 10$ Hz, 1H, $\text{CH}=\text{CHCO}$), 5.90 (d, $J = 10$ Hz, 1H, $\text{CH}=\text{CHCO}$), 5.80 (dddd, $J = 17, 10, 6.5, 6.5$ Hz, 1H, $\text{CH}=\text{CH}_2$), 5.04 (dddd, $J = 17, 1.5, 1.5, 1.5$ Hz, 1H, *trans* $\text{CH}=\text{CHH}$),

4.96 (dddd, $J = 10, 1.5, 1.5, 1.5$ Hz, 1H, *cis* CH=CHH), 2.45 (m, 2H), 2.15-1.87 (m, 3H), 1.87-1.70 (m, 1H), 1.60-1.48 (m, 2H), 1.15 (s, 3H, CH₃); ¹³C NMR (75 MHz) δ 197.2 (p), 157.1 (a), 138.7 (a), 127.8 (a), 114.6 (p), 40.2 (p), 35.2 (p), 34.3 (p), 33.5 (p), 28.7 (p), 24.6 (a); HRMS M⁺ 164.1199 (calcd for C₁₁H₁₆O: 164.1201). Anal. Calcd for C₁₁H₁₆O: C 80.44, H 9.82. Found: C 80.30, H 9.83.

(4R)-(3-Butenyl)-6-carbomethoxy-4-methyl-2-cyclohexenone (8)

To a stirred suspension of sodium hydride (115 mg, 95%, 4.55 mmol) in dry dimethyl carbonate (7 mL) at rt under argon, was added a solution of (+)-**7** (300 mg, 1.83 mmol) in dimethyl carbonate (3 mL). The reaction mixture was refluxed for 1 h and then cooled down to 0 °C. A 1 N HCl solution (10 mL) was added cautiously to the mixture. The resulting mixture was extracted with ether (3 x 50 mL). The combined extracts were washed with water and brine, dried over MgSO₄ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography with ethyl acetate/hexane (5:95) to afford (+)-**8** (368 mg, 91%) as a yellowish oil: $[\alpha]_D^{20} = +96.1^\circ$ (c 1.80, EtOH); IR (CH₂Cl₂ cast) 3450 (OH, enol), 1747 (C=O, ester), 1694 (C=O, ketone), 1662 (C=O, enol ester) and 1626 (C=C, enol) cm⁻¹; ¹H NMR (200 MHz) a mixture of three isomers (two epimers and an enol) in a ratio of 1:1:3: δ 11.87 (s, 0.6H, OH), 6.70 (dd, $J = 10, 1.5$ Hz, 0.2H, CH=CHCO), 6.69 (dd, $J = 10, 1.5$ Hz, 0.2H, CH=CHCO), 6.05 (d, $J = 10$ Hz, 0.6H, CH=CHCO, enol form), 5.91 (d, $J = 10$ Hz, 0.2H, CH=CHCO), 5.86 (d, $J = 10$ Hz, 0.6H, CH=CHCO, enol form), 5.73 (d, $J = 10$ Hz, 0.2H, CH=CHCO), 5.66-5.85 (m, 1H, CH=CH₂), 4.90-5.15 (m, 2H, CH=CH₂), 3.76, 3.75 (s, 3H, OCH₃), 3.65-3.45 (m, 0.4H, COCHCOOMe), 2.50-1.85 (m, 4H), 1.75-1.35 (m, 2H), 1.18, 1.15, 1.02 (s, 3H, CH₃); HRMS M⁺ 222.1256 (calcd for C₁₃H₁₈O₃: 222.1256). Anal. Calcd for C₁₃H₁₈O₃: C 70.24, H 8.16. Found: C 70.20, H 8.25.

(S)-4-(3-Butenyl)-2-carbomethoxy-4-methyl-2,5-cyclohexadienone (9)

To a solution of (+)-**8** (200 mg, 0.9 mmol) in dry benzene (10 mL) at rt under argon, was added DDQ (407 mg, 1.8 mmol). The mixture was stirred for 15 min and then refluxed for 5 h. The reaction mixture was cooled and concentrated. The precipitate was removed by filtration after chloroform (15 mL) was added to the residue. The filtrate was concentrated and the residue

was subjected to flash chromatography with ethyl acetate/hexane (20:80) to give (+)-**9** (173 mg, 87%) as a colorless oil: $[\alpha]_{\text{D}}^{20} = +27.8^\circ$ (c 1.60, EtOH); IR (CH_2Cl_2) 1742 (C=O, ester), 1665 (C=O, ketone) and 1638 (C=C) cm^{-1} ; ^1H NMR (200 MHz) δ 7.50 (d, $J = 3$ Hz, 1H, $\text{CH}=\text{CCOOMe}$), 6.75 (dd, $J = 10, 3$ Hz, 1H, $\text{CH}=\text{CHCO}$), 6.32 (d, $J = 10$ Hz, 1H, $\text{CH}=\text{CHCO}$), 5.70 (dddd, $J = 17, 10, 6.5, 6.5$ Hz, 1H, $\text{CH}=\text{CH}_2$), 4.97 (dddd, $J = 17, 1.5, 1.5, 1.5$ Hz, 1H, *trans* $\text{CH}=\text{CHH}$), 4.95 (dddd, $J = 10, 1.5, 1.5, 1.5$ Hz, 1H, *cis* $\text{CH}=\text{CHH}$), 3.87 (s, 3 H, OCH_3), 1.95-1.75 (m, 4H), 1.31 (s, 3H, CH_3); ^{13}C NMR (75 MHz) δ 181.6 (p), 165.2 (p), 160.6 (a), 153.6 (a), 137.2 (a), 131.8 (p), 129.7 (a), 115.5 (p), 52.4 (p), 42.1 (a), 39.7 (a), 29.3 (a), 25.7 (p); HRMS M^+ 220.1098 (calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$: 220.1099). Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$: C 70.89, H 7.32. Found: C 70.57, H 7.41.

(1R, 6R, 9S)-2-Carbomethoxy-9-iodo-6-methylbicyclo[4.4.0]dec-4-en-3-one (2)

To a stirred suspension of anhydrous zinc iodide (80 mg, 0.26 mmol) in dry ether (10 mL) at rt under argon, was added a solution of (+)-**9** (46 mg, 0.21 mmol) in ether (5 mL). The reaction flask was protected from light. The reaction mixture was stirred for 3 days. A 1 N HCl solution (20 mL) was added. The resulting mixture was extracted with ether (3 x 50 mL). The extracts were washed with water and brine, dried over MgSO_4 , filtered and concentrated. The crude product was purified by flash chromatography using ethyl acetate/hexane (5:95) to afford the bicyclic iodide **2** (60 mg, 82%) as a colorless oil: $[\alpha]_{\text{D}}^{20} = -142.4^\circ$ (c 0.70, EtOH); IR (CH_2Cl_2 cast) 3200 (OH, enol), 1733 (C=O, ester), 1683 (C=O, ketone), 1652 (C=O, enol ester) and 1625 (C=C, enol) cm^{-1} ; ^1H NMR (300 MHz) a mixture of three isomers in a ratio of 1:1:4.7: δ 11.85 (s, 0.7H, OH), 6.10-5.95 (m, 2H, $\text{CH}=\text{CH}$), 4.00 (dddd, $J = 12, 12, 4, 4$ Hz, 1H, CHI), 3.70-3.85 (m, 3.3H, OCH_3 and COCHCOOMe), 2.30-2.50 (m, 2H), 1.80-2.15 (m, 2H), 1.30-1.65 (m, 3H), 1.08, 1.02, 0.95 (s, 3H, CH_3); ^{13}C NMR (75 MHz) δ 172.4 (p), 165.0 (p), 147.9 (a), 123.2 (a), 97.9 (p), 51.6 (a), 42.0 (a), 41.9 (p), 40.7 (p), 37.7 (p), 36.2 (p), 26.7 (a), 25.9 (a); HRMS M^+ 348.0222 (calcd for $\text{C}_{13}\text{H}_{17}\text{O}_3\text{I}$: 348.0223). Anal. Calcd for $\text{C}_{13}\text{H}_{17}\text{O}_3\text{I}$: C 44.85, H 4.92. Found: C 44.57, H 5.16.

(1S, 6R, 8S)-4-Acetoxy-5-carbomethoxy-8-iodo-1-methylbicyclo[4.4.0]deca-2,4-diene (10)

To a solution of (-)-**2** (50 mg, 0.14 mmol) in pyridine (2 mL) at rt under argon, was added acetic anhydride (0.5 mL, 5.3 mmol). The reaction mixture was stirred overnight. Pyridine was removed under reduced pressure. The residue was extracted with ether (3 x 50 mL). The extracts were washed with 1N hydrochloric acid and brine, dried over MgSO₄, filtered and concentrated. Flash chromatography of the residue with ethyl acetate/hexane (5:95) gave enol acetate (**10**) (49.9 mg, 89%) as a colorless oil: $[\alpha]_D^{20} = -200.2^\circ$ (c 2.60, EtOH); IR (CH₂Cl₂ cast) 1765 (CH₃CO) and 1709 (COOCH₃) cm⁻¹; ¹H NMR (200 MHz) δ 6.00 (dd, J = 9.5, 1.5 Hz, 1H, CH=CHCO), 5.80 (d, J = 9.5 Hz, 1H, CH=CHCO), 4.00 (dddd, J = 12, 12, 4, 4 Hz, 1H, CHI), 3.75 (s, 3H, OCH₃), 2.60 (ddd, J = 12, 4, 1.5 Hz, 1H, ring junction proton), 2.50 (m, 1H, **H7e**), 2.36 (m, 1H, **H9e**), 2.20 (s, 3H, CH₃CO), 1.82-2.10 (m, 2H, **H7a** + **H10e**), 1.58 (m, 1H, **H9a**), 1.43 (m, 1H, **H10a**), 0.95 (s, 3H, CH₃); ¹³C NMR (75 MHz) δ 168.5 (p), 165.4 (p), 151.6 (p), 145.0 (a), 123.8 (a), 116.2 (p), 56.5 (a), 51.9 (a), 42.4 (a), 38.1 (p), 37.0 (p), 35.9 (p), 34.4 (p), 25.3 (a), 20.9 (a); HRMS M⁺ 390.0325 (calcd for C₁₅H₁₉O₄I: 390.0328). Anal. Calcd for C₁₅H₁₉O₄I: C 60.30, H 6.41. Found: C 60.24, H 6.46.

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REFERENCE

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