The Catalytic Asymmetric Total Synthesis of Elatol

David E. White, Ian C. Stewart, Robert H. Grubbs, and Brian M. Stoltz*

The Arnold and Mabel Beckman Laboratories of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, USA

Supporting Information

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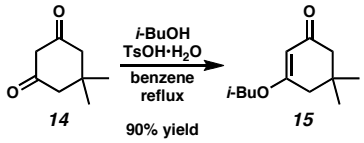
Materials and Methods

Unless stated otherwise, reactions were conducted under an ambient atmosphere. Anhydrous solvents were prepared by passing the solvents through activated alumina columns. Commercially obtained reagents were used as received, unless specified otherwise. Anhydrous diisopropylamine, triethylamine, and *N,N,N′,N′*-tetramethylethylenediamine were obtained from distillation over CaH_2. Methyl vinyl ketone was distilled prior to use. Phosphinooxazoline ligand **18** was prepared according to the previously published method.[1] Anhydrous $CeCl_3$ was prepared according to the method of Imamoto.[2] Salt **S5** was prepared according to the method of Drauz.[3] Phosphine **S8**[4] was prepared according to the method of Bussaca.[5] Thin-layer

(1) Tani, K.; Behenna, D. C.; McFadden, R. M.; Stoltz, B. M. *Org. Lett.* **2007**, *9*, 2529–2531.
(2) Takeda, N.; Imamoto, T. *Organic Syntheses;* Wiley & Sons: New York, 2004, Collect. Vol. X, pp 200–204.
(3) Drauz, K.; Jahn, W.; Schwarm. M. *Chem. Eur. J.* **1995**, *1*, 538–540
(4) van Doorn, J. A.; Meijboom, N. *Recl. Trav. Chim. Pays-Bas* **1992**, *111*, 170–177.

chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates [0.25 mm (analytical) or 0.5 mm (preparative)] and visualized using a combination of UV light (254 nm), *p*-anisaldehyde staining, and potassium permanganate staining. TLC data include R_f and eluent (% by volume). ICN silica gel (particle size 0.032-0.063 mm), SiliCycle® Silia*Flash*® P60 Academic Silica Gel (particle size 40-63 μm; pore diameter 60 Å), or Florisil® (100–200 mesh) were used for flash column chromatography. All flash column chromatographic purification steps are reported as follows: size of immobile phase column (length x diameter) and eluent (% by volume). Analytical chiral HPLC analyses were performed with an Agilent 1100 Series HPLC instrument. Preparative HPLC purifications were performed with a Beckman System Gold® or an Agilent 1200 Series HPLC instrument. ^{1}H NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz) or a Varian Inova 500 (at 500 MHz) instrument and are reported relative to the residual solvent peak (δ 7.26 for $CDCl_3$ and δ 2.05 for acetone-d_6) or Me_4Si (δ 0.00) in the case of CCl_4. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. ^{13}C NMR spectra were recorded on a Varian Mercury 300 (at 75 MHz), or a Varian Inova 500 (at 126 MHz) instrument and are reported relative the residual solvent peak (δ 77.0 for $CDCl_3$). Data for ^{13}C NMR spectra are reported in terms of chemical shift (δ ppm). ^{19}F NMR spectra were recorded on a Varian Inova 500 (at 470 MHz) instrument and are reported in terms of chemical shift (δ ppm) without the use of a reference peak. IR spectra were recorded on a Perkin Elmer Spectrum BXII spectrometer and are reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-1010 polarimeter, using a 100 mm path-length cell. High-resolution mass spectra were obtained from the California Institute of Technology Mass Spectral Facility.

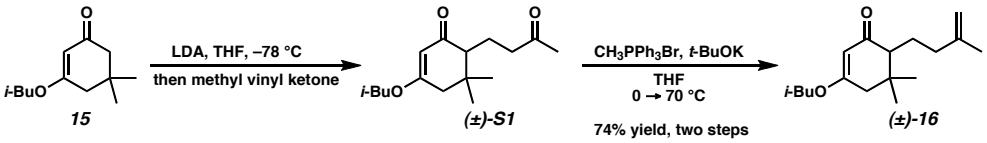
Procedures for the Synthesis of (+)-Laurencenone B and (+)-Elatol



Vinylogous ester 15.[6] To a 500 mL round-bottomed flask equipped with a magnetic stir bar, a Dean-Stark trap, and a condenser was added dimedone **14** (10.0 g, 71.3 mmol), *p*-toluenesulfonic acid monohydrate (269 mg, 1.41 mmol), anhydrous benzene (120 mL), and isobutanol (33.0 mL, 358 mmol). The resulting solution was then heated to reflux in an oil bath and stirred for 21 h. After cooling to 23 °C, the reaction was washed with saturated $NaHCO_3$ (aq) (100 mL), and the aqueous layer was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine (2 x

(5) Busacca, C. A.; Lorenz, J. C.; Grinberg, N.; Haddad, N.; Hrapchak, M.; Latli, B.; Lee, H.; Sabila, P.; Saha, A.; Sarvestani, M.; Shen, S.; Varsolona, R.; Wei, X.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 4277–4280.
(6) House, H. O.; Fischer, W. F., Jr. *J. Org. Chem.* **1968**, *33*, 949–956.

100 mL) and dried over $MgSO_4$. Solvent was removed under reduced pressure, and the crude product mixture was azeotroped with toluene (4x) to remove excess isobutyl alcohol. The product was then distilled at 109–110 °C and 1.3 torr to provide vinylogous ester **15**[6] (12.561 g, 90%) as a slightly yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.33 (br s, 1H), 3.60 (d, *J* = 6.6 Hz, 2H), 2.28 (s, 2H), 2.21 (s, 2H), 2.03 (app. septet, *J* = 6.7 Hz, 1H), 1.07 (s, 6H), 0.97 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.6, 176.4, 101.4, 74.7, 50.7, 42.8, 32.4, 28.3, 27.7, 19.0; IR (neat film, NaCl) ν 2961, 2876, 1660, 1608, 1471, 1404, 1382, 1367, 1320, 1221, 1162, 1145, 1014, 992, 822 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{12}H_{20}O_2$ $[M]^+$: 196.1463, found 196.1463.

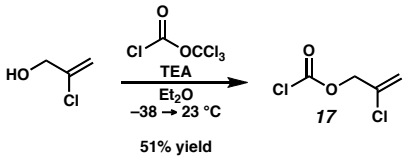


Olefin (±)-16. *Part 1: Alkylation.*[7] A 250 mL two-neck round-bottomed flask equipped with a 25 mL addition funnel, a stir bar, and two septa was flame dried under vacuum. After refilling with Ar, anhydrous THF (95 mL) and anhydrous diisopropylamine (2.0 mL, 14.3 mmol) were added via syringe, and the solution was cooled to 0 °C in an ice bath. *n*-BuLi (2.6 M in hexanes, 5.4 mL, 14.0 mmol) was added dropwise via syringe, and the solution was stirred at 0 °C for 1 h. The resulting LDA solution was then cooled to –78 °C over 16 min. Vinylogous ester **15** (2.50 g, 12.7 mmol) in anhydrous THF (10 mL) was then added dropwise over 16 min via the addition funnel, washing the funnel with THF (5 mL) upon complete addition. A yellow solution was obtained. After stirring at –78 °C for 1 h, methyl vinyl ketone (1.05 mL, 12.9 mmol) was added dropwise quickly via syringe. A slight exotherm was observed. The reaction was stirred for an additional 3 h at –78 °C, at which time H_2O (20 mL) was added. The mixture was warmed to 23 °C, at which time the organic layer was separated. The aqueous layer was extracted with Et_2O (2 x 100 mL) and EtOAc (2 x 100 mL), at which point it was completely incorporated into the organic layers. The combined organic layers were washed sequentially with saturated $NaHCO_3$ (aq) (300 mL) and brine (2 x 300 mL) and then dried over $MgSO_4$. Solvent was removed under reduced pressure to provide 3.469 g of ketone (±)-**S1** as a reddish-orange liquid containing 12.9% by mass starting vinylogous ester **15**, 4.1% by mass EtOAc, and 1% by mass Et_2O as determined by ^{1}H NMR spectroscopy. The crude yield corrected for impurities was 84%. The crude material was carried directly to Part 2. An aliquot from a separate run was purified by preparative thin-layer chromatography (0.25 mm thickness, eluted twice with 30% EtOAc/hexanes eluent). R_f 0.40 (eluting twice with 30% EtOAc/hexanes eluent); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.20 (s, 1H), 3.57 (dd, *J* = 9.4, 6.7 Hz, 1H), 3.54 (dd, *J* = 9.5, 6.6 Hz, 1H), 2.64 (ddd, *J* = 18.2, 9.0, 5.2 Hz, 1H), 2.51 (ddd, *J* = 18.3, 9.0, 6.6 Hz, 1H), 2.36 (d, *J* = 17.8, 1H), 2.19 (d, *J* = 17.6 Hz, 1H), 2.13 (s, 3H), 2.01 (app. septet, *J* = 6.7 Hz, 1H), 1.82–1.92 (m, 2H), 1.53–1.64 (m, 1H), 1.08 (s, 3H), 1.00 (s, 3H), 0.96 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.1, 202.6, 175.0, 100.4, 74.6, 55.9, 42.2, 41.3, 35.0, 30.2, 28.5, 27.7, 24.6, 20.0, 19.1; IR (neat film, NaCl) ν 2962, 2934, 2897, 2876, 1716, 1652, 1611, 1471, 1424, 1406, 1382, 1366, 1324, 1298, 1276, 1221, 1199,

(7) Takahashi, K.; Tanaka, T.; Suzuki, T.; Hirama, M. *Tetrahedron* **1994**, *50*, 1327–1340.

1179, 1155, 1131, 1067, 1056, 1008, 994, 968, 952, 912, 904, 851, 831, 745, 710, 693, 627 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{16}H_{26}O_3$ $[M]^+$: 266.1882, found 266.1928.

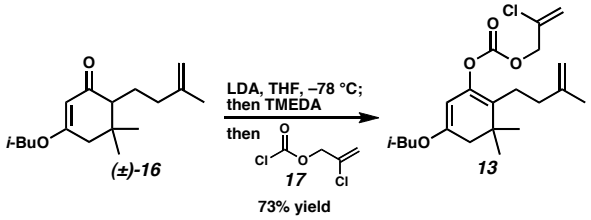
Part 2: Wittig Olefination. To a flame-dried 500 mL round-bottomed flask equipped with a magnetic stir bar was added methyltriphenylphosphonium bromide (8.00 g, 22.4 mmol). After attaching an oven-dried condenser and sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous THF (255 mL) was added via syringe, and the mixture was cooled to 0 °C in an ice bath. Potassium *tert*-butoxide (2.39 g, 21.5 mmol) was added under positive Ar pressure to give a yellow mixture, and the system was flushed with Ar while being allowed to warm to 23 °C over 25 min. The crude ketone (±)-**S1** from Part 1 (3.461 g, 82% pure by mass, 10.7 mmol) in anhydrous THF (5 mL) was then added via syringe, washing the original flask with THF (5 mL). The reaction was placed in a 70 °C oil bath and stirred for 2 h. After cooling to 23 °C, the reaction mixture was filtered through a pad of silica gel (2.5 x 10 cm), eluting with THF (1 L). Solvent was removed under reduced pressure. Flash chromatography over silica gel (9 x 5 cm, 20% Et_2O/pentane eluent) then provided olefin (±)-**16** (2.489 g, 74% over two steps) as a slightly yellow liquid. The isolated yield for Part 2 corrected for impurities in the crude ketone (±)-**S1** was 88%. R_f 0.33 (20% Et_2O/pentane eluent); ^1H NMR (500 MHz, $CDCl_3$) δ 5.23 (s, 1H), 4.69–4.73 (m, 1H), 4.66–4.69 (m, 1H), 3.57 (d, *J* = 6.4 Hz, 2H), 2.33 (d, *J* = 17.6 Hz, 1H), 2.20 (d, *J* = 17.6 Hz, 1H), 2.08-2.19 (m, 1H), 1.960–2.07 (m, 2H), 1.90–1.96 (m, 1H), 1.72 (s, 3H), 1.55–1.69 (m, 2H), 1.07 (s, 3H), 0.98 (s, 3H), 0.96 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.3, 174.3, 145.9, 109.9, 100.6, 74.6, 56.3, 41.7, 36.6, 35.1, 28.6, 27.7, 24.6, 24.1, 22.6, 19.1; IR (neat film, NaCl) ν 2961, 2933, 2875, 1656, 1613, 1471, 1424, 1404, 1382, 1365, 1297, 1220, 1191, 1153, 1007, 885, 832 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{17}H_{28}O_2$ $[M]^+$: 264.2089, found 264.2081.



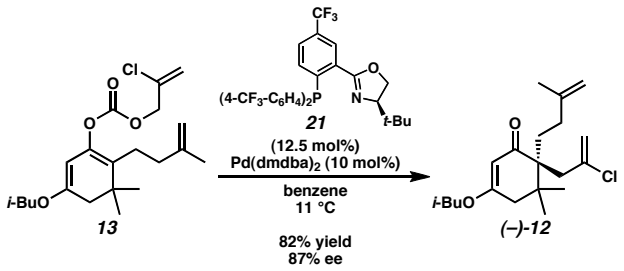
Chloroformate 17.[8] A 500 mL three-neck round-bottomed flask equipped with a 250 mL addition funnel, a stir bar, and three septa was flame dried under vacuum. After refilling with Ar, anhydrous Et_2O (30 mL) was added via syringe, and the system was cooled to approx. –10 °C. Diphosgene (7.7 mL, 63.8 mmol) was added dropwise via syringe, and the solution was cooled to approx. –20 °C. 2-Chloroallyl alcohol (5.0 mL, 62.8 mmol) in anhydrous Et_2O (75 mL) was added dropwise via the addition funnel, and the solution was stirred at approx. –20 °C for an additional 15 min. The reaction was cooled to approx. –30 °C, and triethylamine (8.8 mL, 63.1 mmol) in anhydrous Et_2O (75 mL) was added dropwise via the addition funnel, generating a white precipitate. The reaction was then cooled to approx. –38 °C and stirred for 3 h, at which time it was allowed to warm to 23 °C while stirring for an additional 15 h. During this time, the reaction mixture became very thick, and anhydrous Et_2O (50 mL) was added to obtain a stirable suspension. Ar was bubbled through the suspension for 2 h to remove excess phosgene, employing a saturated $NaHCO_3$ (aq)/triethylamine trap. The reaction mixture

(8) Apparu, M.; Tiba, Y. B.; Léo, P.-M.; Fagret, D. *Eur. J. Org. Chem.* **2000**, 1007–1012.

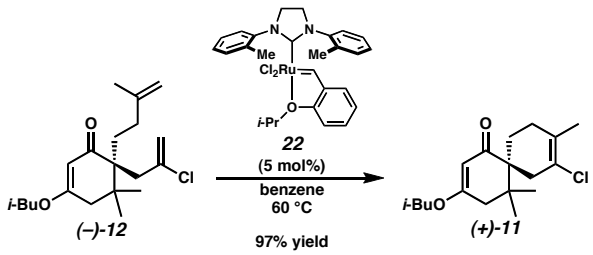
was filtered via vacuum filtration through a fritted funnel, and the filtrate was concentrated by rotary evaporation under reduced pressure. The product was then distilled at 50 °C and 20 torr to provide chloroformate **17** (4.987 g, 51%) as a colorless liquid containing a minor unidentified impurity (1% by area) by ^{1}H NMR spectroscopy; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.58 (dt, *J* = 2.0, 1.0 Hz, 1H), 5.53 (d, *J* = 2.2 Hz, 1H), 4.84 (d, *J* = 0.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 133.5, 117.4, 72.2; IR ($CHCl_3$, KBr) ν 1775 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_4H_4Cl_2O_2$ [M]$^+$: 153.9588, found 153.9593.



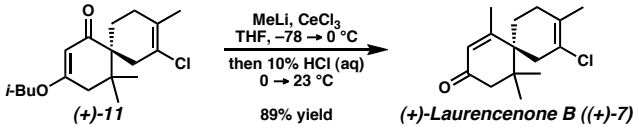
Enol carbonate 13. A 250 mL two-neck round-bottomed flask equipped with a 50 mL addition funnel, a stir bar, and two septa was flame dried under vacuum. After refilling with Ar, anhydrous THF (55 mL) and anhydrous diisopropyl amine (1.45 mL, 10.3 mmol) were added via syringe, and the solution was cooled to 0 °C in an ice bath. *n*-BuLi (2.5 M in hexanes, 3.8 mL, 9.5 mmol) was added dropwise via syringe, and the solution was stirred at 0 °C for 30 min. The resulting LDA solution was then cooled to –78 °C over 15 min. Olefin (±)-**16** (2.282 g, 8.63 mmol) in anhydrous THF (10 mL) was then added dropwise over 26 min via the addition funnel, washing the funnel with THF (5 mL) upon complete addition. A yellow solution was obtained. After stirring at –78 °C for 1 h, *N,N,N′,N′*-tetramethylethylenediamine (1.55 mL, 10.3 mmol) was added dropwise over 2 min via syringe. After stirring at –78 °C for an additional 1 h, chloroformate **17** (1.471 g, 9.49 mmol) in anhydrous THF (10 mL) was then added dropwise over 22 min via the addition funnel, washing the funnel with THF (5 mL) upon complete addition. A visible exotherm was observed, and the solution changed from yellow to brownish-red in color. The reaction was stirred for an additional 3 h at –78 °C, at which time saturated $NaHCO_3$ (aq) (35 mL) and H_2O (35 mL) were added. The mixture was allowed to warm to 23 °C, at which time the organic layer was immediately separated. The aqueous layer was extracted with Et_2O (2 x 200 mL), and the combined organic layers were washed with brine (2 x 200 mL) and dried over $MgSO_4$. Solvent was removed under reduced pressure. Flash chromatography over Florisil® (12 x 5 cm, 2.5% Et_2O/petroleum ether eluent) then provided enol carbonate **13** (2.412 g, 73%) as a colorless liquid containing minor unidentified impurities (2% by area) by ^{1}H NMR spectroscopy. R_f 0.17 (2.5% Et_2O/petroleum ether eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.52–5.56 (m, 1H), 5.43–5.46 (m, 1H), 4.76 (s, 1 H), 4.71–4.74 (m, 2H), 4.66–4.72 (br m, 2H), 3.48 (d, *J* = 6.6 Hz, 2H), 2.19 (s, 2H), 2.01–2.19 (m, 4H), 1.97 (app. septet, *J* = 6.7 Hz, 1H), 1.74 (br s, 3H), 1.09, (s, 6H), 0.94 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7, 153.0, 145.9, 142.0, 135.2, 123.3, 115.2, 109.8, 91.1, 73.9, 69.1, 43.4, 37.9, 35.4, 27.9, 26.0, 24.2, 22.4, 19.2; IR (neat film, NaCl) ν 3074, 2960, 2873, 1762, 1662, 1622, 1470, 1382, 1365, 1329, 1276, 1240, 1183, 1160, 1100, 1046, 1024, 972, 952, 922, 888, 782, 639 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{21}H_{31}ClO_4$ [M]$^+$: 382.1911, found 382.1912.



α,ω-Diene (–)-12. To a flame-dried 500 mL round-bottomed flask equipped with a magnetic stir bar was added phosphinooxazoline ligand **21** (0.36 g, 0.67 mmol) and bis(3,5,3′,5′-dimethoxydibenzylideneacetone)palladium(0) (0.44 g, 0.54 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (150 mL, deoxygenated prior to use by sparging with N_2 in a flame-dried flask for ≥1 h) was added via syringe, and the resulting solution was stirred for 30 min at 23 °C, during which time it turned dark yellow-brown. The solution was cooled in an ice bath until it just begins to freeze (7 min) and was then transfered to an 11 °C cooling bath. Concurrently, a second flame-dried round bottomed flask was charged with enol carbonate **13** (2.056 g, 5.37 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Deoxygenated anhydrous benzene (6.5 mL) was added via syringe, and the resulting solution was cooled in an ice bath, becoming very viscous at this time. The enol carbonate solution was then transferred via syringe to the catalyst solution at 11 °C, washing the original flask with deoxygenated anhydrous benzene (6.5 mL, allowed to cool briefly before transferring). The reaction, which turned green, was then stirred at 11 °C for 24 h. Solvent was removed under reduced pressure. The residue was suspended in Et_2O and filtered through filter paper to remove precipitated Pd. The filtrate was then concentrated under reduced pressure. The residue was suspended in 5% Et_2O/petroleum ether (some solid precipitates) and applied to a silica gel column (12 x 5 cm). Flash chromatography (5% Et_2O/petroleum ether eluent) then provided α,ω-diene (–)-**12** (1.488 g, 82%) as a highly viscous, slightly yellow oil. Observed 87% ee as determined by chiral HPLC analysis (Chiralpak® AD, 1% EtOH/hexanes, 1 mL/min, 254 nm, t_R (minor) = 6.1 min; t_R (major) = 6.7 min). R_f 0.06 (5% Et_2O/petroleum ether eluent); $[\alpha]^{24}_D$ –10.55° (*c* 0.995, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.30 (br s, 1H), 5.28 (s, 1H), 5.23 (s, 1H), 4.67–4.71 (m, 1H), 4.64–4.68 (m, 1H), 3.59 (dd, *J* = 9.5, 6.6 Hz, 1H), 3.54 (dd, *J* = 9.3, 6.8 Hz, 1H), 2.94–3.18 (br m, 1H), 2.46–2.83 (br m, 1H), 2.57 (br d, *J* = 15.6 Hz, 1H), 2.12–2.38 (br m, 1H), 2.12-2.26 (m, 1H), 1.88–2.12 (br m, 1H), 2.01 (app. septet, *J* = 6.7 Hz, 1H), 1.71 (s, 3H), 1.50–1.82 (br m, 2H), 1.21 (br s, 3H), 1.11 (s, 3H), 0.97 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.6, 172.9, 146.2, 141.7 (br), 116.7, 109.5, 100.2 (br), 74.5, 54.6, 43.1, 38.9, 37.4 (br), 32.9, 28.3, 27.7, 24.8, 24.6, 22.8, 19.0; IR (neat film, NaCl) ν 3073, 2963, 2939, 2877, 1651, 1622, 1471, 1449, 1431, 1406, 1383, 1367, 1298, 1222, 1206, 1172, 1157, 1134, 1069, 1009, 967, 956, 884, 845, 767, 752, 692, 656, 624 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{20}H_{31}ClO_2$ $[M]^+$: 338.2013, found 338.2009.



Chloroalkene (+)-11. To a flame-dried 100 mL round-bottomed flask equipped with a magnetic stir bar was added catalyst **22** (124.9 mg, 0.219 mmol). After attaching an oven-dried condenser and sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (26 mL, deoxygenated prior to use by sparging with N_2 in a flame-dried flask for ≥1 h) was added via syringe. To the resulting solution was added α,ω-diene (–)-**12** (1.483 g, 4.38 mmol) in deoxygenated anhydrous benzene (6 mL) via syringe, washing the original flask with deoxygenated anhydrous benzene (2 x 6 mL). The reaction was placed in a 60 °C oil bath and stirred for 18 h. After cooling to 23 °C, solvent was removed under reduced pressure. Flash chromatography over silica gel (12 x 5 cm, 20% Et_2O/petroleum ether eluent until product begins to elute, then 30% Et_2O/petroleum ether eluent) then provided chloroalkene (+)-**11** (1.313 g, 97%) as an off-white waxy powder. R_f 0.38 (20% Et_2O/petroleum ether eluent); $[\alpha]^{24}_D$ +99.27° (*c* 1.005, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.19–5.23 (m, 1H), 3.59 (dd, *J* = 9.3, 6.3 Hz, 1H), 3.52 (dd, *J* = 9.5, 6.6 Hz, 1H), 2.50–2.70 (br m, 1H), 2.47 (br d, *J* = 17.1 Hz, 1H), 2.19–2.33 (br m, 1H), 1.61–2.14 (br m, 5 H), 2.01 (app. septet, *J* = 6.7 Hz, 1H), 1.76 (br s, 3H), 1.06 (s, 3H), 0.97 (d, *J* = 6.8 Hz, 6H), 0.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.3, 172.5, 127.3, 125.5 (br), 99.7, 74.5, 52.6, 41.5, 37.5, 34.4 (br), 29.5, 27.7, 25.7 (br), 24.1, 23.8, 19.7, 19.1; IR (neat film, NaCl) ν 2961, 2931, 2876, 2838, 1657, 1618, 1470, 1434, 1404, 1383, 1365, 1344, 1297, 1220, 1169, 1137, 1045, 1008, 965, 908, 858, 830, 817, 742, 685, 621 cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{18}H_{28}ClO_2$ $[M + H]^+$: 311.1778, found 311.1789.



(+)-Laurencenone B ((+)-7).[9] In a glove box, anhydrous $CeCl_3$ (3.973 g, 16.1 mmol) was added to a flame-dried 250 mL round-bottomed flask equipped with a magnetic stir bar. The flask was sealed with a septum and removed from the glove box. The flask was placed under high vacuum and refilled with Ar. Anhydrous THF (39 mL) was added via syringe, and the suspension was stirred for 3 h at 23 °C. The suspension was cooled to –78 °C over 15 min, and MeLi (1.37 M in Et_2O, 9.0 mL, 12.3 mmol) was added dropwise over 10 min via syringe. An exotherm was observed, and the liquid phase turned yellow. After stirring for 35 min at –78 °C, chloroalkene (+)-**11** (1.286 g, 4.14 mmol) in anhydrous THF (5 mL) was added dropwise over 3 min via syringe, washing the original flask with THF (2 x 4 mL). The reaction was stirred for 30 min at –78 °C and then placed in an ice bath. After stirring an additional 68 min at 0 °C, 10 wt% HCl (aq) (52 mL) was added, during which time a significant exotherm was

(9) Imamoto, T.; Sugiura, Y.; Takiyama, N. *Tetrahedron Lett*. **1984**, *25*, 4233–4236.

observed. The mixture was then allowed to warm to 23 °C as it was stirred for 66 min. The reaction mixture was extracted with Et_2O (3 x 150 mL), and the combined organic layers were washed with brine (2 x 250 mL) and dried over $MgSO_4$. Solvent was removed under reduced pressure. Flash chromatography over silica gel (10 x 4 cm, 15% Et_2O/pentane eluent until product begins to elute, then 30% Et_2O/pentane eluent) then provided (+)-laurencenone B ((+)-**7**) (929 mg, 89%) as a white powder. Discrepancies existed between the published ^{1}H NMR data reported in the original isolation paper and that of the synthetic material.[10] IR data matched that reported for the natural product. No ^{13}C NMR or optical rotation data were reported. ^{1}H NMR, ^{13}C NMR, and IR data matched that reported for semisynthetic material obtained from the degradation of elatol.[11] The optical rotation matched in sign, but not in magnitude. These comparisons are outlined below. R_f 0.26 (30% Et_2O/petroleum ether eluent); $[\alpha]^{24}_D$ +47.08° (*c* 0.36, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 (s, 1H), 2.50–2.69 (br m, 2H), 2.26 (br d, *J* = 18.3 Hz, 1H), 2.13–2.23 (br m, 1H), 1.99–2.14 (br m, 2H), 1.98 (d, *J* = 0.98 Hz, 3H), 1.93 (ddd, *J* = 12.3, 12.3, 5.4, Hz, 1H), 1.81 (br s, 3H), 1.72–1.80 (m, 1H), 1.06 (s, 3H), 0.97(s, 3H); ^{1}H NMR (500 MHz, acetone-d_6) δ 5.80 (s, 1H), 2.52–2.69 (br m, 2H), 2.31 (dd, *J* = 18.1, 0.98 Hz, 1H), 2.19-2.27 (br m, 1H), 2.02–2.16 (br m, 1H), 1.88–2.02 (m, 2H), 1.98 (d, *J* = 1.2 Hz, 3H), 1.76–1.88 (br m, 1H), 1.80 (br s, 3H), 1.09 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.2, 168.6, 129.6, 127.5, 126.2 (br), 48.8, 46.3, 40.4, 36.3, 30.4 (br), 30.1, 24.8, 23.9 (two overlapping CH_3 peaks as determined by gHSQC and DEPT NMR spectroscopy; second peak appears as an upfield shoulder), 19.7; IR (neat film, NaCl) ν 3025, 2963, 2933, 2855, 1667, 1612, 1462, 1439, 1417, 1392, 1375, 1350, 1331, 1319, 1306, 1282, 1257, 1207, 1192, 1171, 1150, 1137, 1125, 1106, 1070, 1048, 1023, 1010, 988, 972, 954, 930, 913, 869, 834, 818, 684 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{15}H_{21}ClO$ $[M]^+$: 252.1281, found 252.1270.

Comparison of Synthetic and Published ^{1}H NMR, ^{13}C NMR, IR, and $[\alpha]_D$ Data

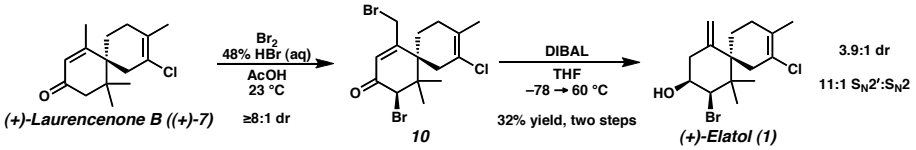
Synthetic	**Natural**[10]
^{1}H NMR (500 MHz, acetone-d_6)	*^{1}H NMR (60, 250, or 360 MHz, acetone-d_6)*
(δ)	(δ)
5.80 (s, 1H)	5.90 (br s, 1H)
2.52–2.69 (br m, 2H)	2.70 (d, *J* = 18 Hz, 1H)
2.31 (dd, *J* = 18.1, 0.98 Hz, 1H)	1.6–2.3 (m, 6H)
2.19-2.27 (br m, 1H)	
2.02–2.16 (br m, 1H)	2.10 (d, *J* = 18 Hz, 1H)
1.88–2.02 (m, 2H)	
1.98 (d, *J* = 1.2 Hz, 3H)	1.98 (d, *J* = 2 Hz, 3H)
1.76–1.88 (br m, 1H)	
1.80 (br s, 3H)	1.75 (br d, *J* = ~4 Hz, 3H)
1.09 (s, 3H)	1.03 (s, 3H)
0.96 (s, 3H)	0.98 (s, 3H)

(10) Kennedy, D. J.; Selby, I. A.; Thomson, R. H. *Phytochemistry* **1988**, *27*, 1761–1766.
(11) Brennan, M. R.; Erickson, K. L; Minott, D. A.; Pascoe, K. O. *Phytochemistry* **1987**, *26*, 1053–1057.

IR	*IR*
(cm^{-1}, selected values)	(cm^{-1})
1667	1670

Synthetic	**Semisynthetic**[11]
^{1}H NMR (500 MHz, $CDCl_3$)	*^{1}H NMR (250 MHz, $CDCl_3$)*
(δ)	(δ)
5.89 (s, 1H)	5.89 (br s, 1H)
2.50–2.69 (br m, 2H)	2.59 (AB m, 2H)
2.26 (br d, *J* = 18.3 Hz, 1H)	1.6–2.3 (m, 6H)
2.13–2.23 (br m, 1H)	
1.99–2.14 (br m, 2H)	
1.98 (d, *J* = 0.98 Hz, 3H)	1.98 (d, *J* = 0.9 Hz, 3H)
1.93 (ddd, *J* = 12.3, 12.3, 5.4 Hz, 1H)	
1.81 (br s, 3H)	1.81 (s, 3H)
1.72–1.80 (m, 1H)	
1.06 (s, 3H)	1.07 (s, 3H)
0.97(s, 3H)	0.97 (s, 3H)
^{13}C NMR (126 MHz, $CDCl_3$)	*^{13}C NMR ($CDCl_3$)*
(δ)	(δ)
198.2	198.04
168.6	168.38
129.6	129.64
127.5	127.54
126.2 (br)	126.23
48.8	48.90
46.3	46.38
40.4	40.45
36.3	36.33
30.4 (br)	30.37
30.1	30.22
24.8	24.80
23.9 (two overlapping CH_3 peaks)	23.89
	23.81
19.7	19.69
IR	*IR*
(cm^{-1}, selected values)	(cm^{-1})
3025	3000
2963	2950
2933	2900
2911 (shoulder)	
2880 (shoulder)	
2855	2850

1667	1660
1612	1610
$[\alpha]^{24}_{D}$	$[\alpha]^{25}_{D}$
+47.08° (c = 0.36, $CHCl_3$)	+58.3° (c = 0.36, $CHCl_3$)



(+)-**Elatol (1).** *Part 1: Bromination.*[12] A half-dram screw-cap vial equipped with a stir bar and a septum-bearing cap was charged with (+)-laurencenone B ((+)-**7**) (9.9 mg, 0.0392 mmol). A solution of 48% HBr (aq) in glacial acetic acid (250:1 v/v AcOH:48% HBr (aq), 0.2 mL) was then added. To the resulting solution was added in one portion a stock solution of bromine in 250:1 v/v AcOH:48% HBr (aq) (0.501 M, 157.5 μL, 0.0789 mmol), resulting in a deep red color. After stirring for approx. 10 min, the reaction turned an orange-red color. After stirring for a total of 31 min, the solution was added to ice water (5 mL). The resulting mixture was extracted with Et_2O (4 x 10 mL), and the combined organic layers were washed with saturated $NaHCO_3$ (aq) (2 x 20 mL) and brine (2 x 20 mL). After drying over $MgSO_4$, solvent was removed under reduced pressure, ultimately isolating the crude dibromide **10** in a 1 dram screw-cap vial. The crude material was carried directly to Part 2. A second run was partially purified (approx. 93% pure by area by ^{1}H NMR spectroscopy) by preparative HPLC (Phenomenex® Gemini™, 25→100% CH_3CN/0.1% TFA (aq), 18 mL/min, 250 nm, t_R = 70–72 min). ^{1}H NMR (500 MHz, C_6D_6) δ 6.05 (s, 1H), 4.55 (s, 1H), 3.67 (d, J = 10.7 Hz, 1H), 3.36–3.41 (m, 1H), 2.56–2.67 (m, 1H), 2.22–2.32 (br m, 1H), 1.52–1.56 (br m, 3H), 1.35–1.44 (br m, 1H), 1.14–1.25 (br m, 1H), 1.08 (ddd, J = 12.5, 12.5, 5.1 Hz, 1H), 0.80 (s, 3H), 0.68–0.76 (br m, 1H), 0.74 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.1, 164.1, 129.9, 129.8, 126.1, 65.7, 49.1, 47.1, 36.5, 30.9, 30.3, 29.7, 24.3, 19.8, 18.7; IR (neat film, NaCl) ν 2979, 2932, 1678, 1438, 1396, 1376, 1284, 1251, 1216, 1170, 1133, 1007, 911, 868, 818, 760, 733 cm^{-1}; HRMS (EI+) m/z calcd. for $C_{15}H_{19}ClOBr^{81}Br$ $[M]^+$: 409.9471, found 409.9482. A minor diastereomer was not isolated. The dr was determined to be ≥8:1 by ^{1}H NMR spectroscopic analysis of the crude product of a third run. This minimal value was based upon resonances that could not be ruled out as corresponding to a minor diastereomer based on the preparative HPLC separation above.

Part 2: Reduction.[13] The 1 dram screw-cap vial containing the crude dibromide **10** from Part 1 was equipped with a stir bar and a septum-bearing cap and placed under high vacuum. After refilling with Ar, anhydrous THF (0.3 mL) was added via syringe, and the solution was cooled to –78 °C. Concurrently, a second 1 dram screw-cap vial equipped with a septum-bearing cap was flame-dried under high vacuum and refilled with Ar. A stock solution of diisobutylaluminum hydride in anhydrous THF (1.59 M,

(12) Kurzer, F.; Patel, J. N. *Monatsh. Chem.* **1987**, *118*, 793–812.
(13) Nakamura, Y.; Okada, M.; Horikawa, H.; Taguchi, T. *J. Fluorine Chem.* **2002**, *117*, 143–148.

0.15 mL, 0.239 mmol) was added via syringe, and the solution was cooled to –78 °C. The precooled stock solution was then added to the crude dibromide **10** solution at –78 °C in one portion via cannula under positive N_2 pressure, at which point gas evolution was observed. The colorless solution was stirred for 2 h at –78 °C, at which point the reaction was placed in a 60 °C heating block, and the Ar inlet was removed. After stirring for an additional 2 h at 60 °C, the reaction was cooled to 23 °C with the aid of a 23 °C water bath. Et_2O (0.5 mL) was added, and the reaction was quenched with a saturated solution of potassium sodium tartrate (aq) (0.5 mL), at which point gas evolution was observed. After stirring vigorously for 1 h, the opaque biphasic mixture was transferred to a 25 mL round-bottomed flask with Et_2O (5 mL) and a saturated solution of potassium sodium tartrate (aq) (5 mL). The mixture was then stirred vigorously until both layers were transparent. The organic layer was separated, and the aqueous layer was extracted with Et_2O (2 x 10 mL). The combined organic layers were washed with brine (2 x 20 mL) and dried over $MgSO_4$. Solvent was removed under reduced pressure. The ratio of S_N2':S_N2 reduction was determined to be 11:1 by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. The crude product was azeotroped with hexanes (4x) and then subjected to preparative thin-layer chromatography (0.5 mm thickness, eluted four times with 15% Et_2O/petroleum ether eluent, then once with 15% EtOAc/hexanes eluent). The product was extracted from the silica with EtOAc and azeotroped with hexanes (3x). Finally, flash chromatography over silica gel (5.3 x 0.5 cm, 5% EtOAc/hexanes eluent until product begins to elute, then 30% EtOAc/hexanes eluent) then provided (+)-elatol ((+)-**1**) (4.4 mg) as a colorless oil containing 6% of the undesired S_N2 reduction product by ^{1}H NMR spectroscopy. The corrected yield was 32% over two steps. The dr of the initial ketone reduction was determined to be 3.9:1 syn:anti (relative to the bromide) by ^{1}H NMR spectroscopic analysis of the crude product of separate run quenched at –78 °C after 2 h. ^{1}H NMR data matched that reported in the original isolation paper,[14] and this comparison is outlined below. R_f 0.64 (eluted four times with 15% Et_2O/petroleum ether eluent, then once with 15% EtOAc/hexanes eluent); $[\alpha]^{23}_D$ +92.09° (*c* 0.22, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.13 (s, 1H), 4.80 (s, 1H), 4.61 (d, *J* = 2.9 Hz, 1H), 4.13–4.17 (m, 1H), 2.55–2.66 (br m, 2H), 2.51 (dd, *J* = 14.6, 2.7 Hz, 1H), 2.33–2.41 (br m, 1H), 2.16–2.20 (m, 1H), 1.92–2.00 (br m, 1H), 1.75–1.86 (br m, 2H), 1.70 (br s, 3H), 1.58–1.67 (m, 1H), 1.08 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.7, 128.1, 124.1, 115.9, 72.2, 70.9, 49.1, 43.1, 38.6, 37.9, 29.3, 25.6, 24.2, 20.8, 19.4; IR (neat film, NaCl) ν 3564, 3475, 3086, 2975, 2949, 2913, 2831, 1808, 1724, 1681, 1643, 1470, 1453, 1430, 1394, 1372, 1354, 1340, 1319, 1292, 1254, 1225, 1207, 1188, 1165, 1141, 1130, 1106, 1086, 1073, 1031, 1014, 982, 956, 943, 897, 879, 826, 811, 761, 737, 685, 706, 667, 642, 615 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{15}H_{22}BrClO$ [M]$^+$: 332.0543, found 332.0546.

Comparison of Synthetic and Published (Original Isolation) ^{1}H NMR Data

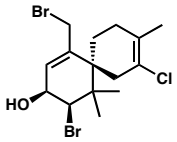
Synthetic	**Natural[14]**
^{1}H NMR (500 MHz, $CDCl_3$)	*^{1}H NMR (100 MHz, $CDCl_3$)*
(selected values)	*(published values from original isolation)*

(14) Sims, J. J.; Lin, G. H. Y.; Wing, R. M. *Tetrahedron Lett.* **1974**, *15*, 3487–3490.

(δ)	(δ)
5.13 (s, 1H)	5.12 (s, 1H)
4.80 (s, 1H)	4.80 (s, 1H)
4.61 (d, *J* = 2.9 Hz, 1H)	4.60 (d, *J* = 3 Hz, 1H)
4.13–4.17 (m, 1H)	4.16 (m, 1H)
1.70 (br s, 3H)	1.70 (m, 3H)
1.08 (s, 3H)	1.10 (s, 6H)
1.07 (s, 3H)	

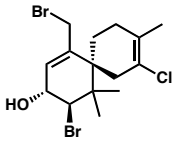
Analysis of a natural sample of elatol (1). A natural sample of elatol (**1**) provided by Prof. Mercedes Cueto was identical in all respects to the synthetic material except for its optical rotation: $[\alpha]^{25}_{D}$ +109.78° (*c* 0.045, $CHCl_3$). Based on 87% ee, the expected $[\alpha]_D$ value for the synthetic material would be +95.5°, which differed from the observed value by 3.6%.

Characterization data for initial ketone reduction diastereomers.



i

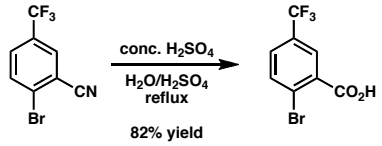
***cis*-Bromohydrin i**: R_f 0.54 (30% EtOAc/hexanes eluent); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.14 (d, *J* = 3.9 Hz, 1H), 4.79 (d, *J* = 5.1 Hz, 1H), 4.22–4.27 (br m, 1H), 4.04–4.11 (m, 2H), 2.73–2.81 (br m, 1H), 2.50–2.59 (br m, 1H), 2.38 (d, *J* = 3.4 Hz, 1H), 2.10–2.18 (br m, 1H), 1.92–2.03 (br m, 1H), 1.76-1.85 (m, 4H), 1.53–1.60 (m, 1H), 1.14 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 130.9, 129.6, 127.0, 68.6, 65.9, 47.7, 41.1, 36.9, 33.5, 30.2, 29.8, 24.3, 19.8, 19.0; IR (neat film, NaCl) ν 3541, 3455, 2976, 2932, 1678, 1438, 1219, 731 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{15}H_{21}ClOBr^{81}Br$ $[M]^+$: 411.9627, found 411.9620. The relative stereochemistry of the bromohydrin functionality was established by NOESY1D NMR spectroscopy and subsequent conversion to elatol (**1**).



S2

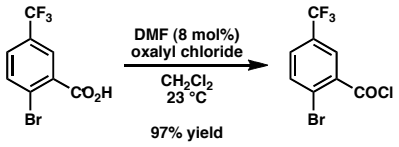
***trans*-Bromohydrin S2**: R_f 0.44 (30% EtOAc/hexanes eluent); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.00 (d, *J* = 3.4 Hz, 1H), 4.48 (d, *J* = 9.0 Hz, 1H), 4.35–4.41 (br m, 1H), 4.03–4.11 (m, 2H), 2.77–2.84 (br m, 1H), 2.54–2.63 (br m, 1H), 2.43 (d, *J* = 3.7 Hz, 1H), 2.10–2.19 (br m, 1H), 1.89–2.00 (br m, 1H), 1.87 (ddd, *J* = 12.2, 12.2, 5.0 Hz, 1H), 1.80–1.84 (br m, 3H), 1.62–1.69 (m, 1H), 1.16, (s, 3H), 1.05 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 131.6, 129.6, 126.9, 73.3, 70.5, 47.4, 44.3, 36.3, 33.8, 31.4, 29.7, 24.6, 19.8, 17.6; IR (neat film, NaCl) ν 3383, 2977, 2932, 1677, 1438, 1039, 733 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{15}H_{21}ClOBr^{81}Br$ $[M]^+$: 411.9627, found 411.9621.

Procedures for the Synthesis of Phosphinooxazoline Ligand 21



S3

2-Bromo-5-(trifluoromethyl)-benzoic acid (S3).[15] A 250 mL round-bottomed flask equipped with a stir bar and a condenser was charged with 2-bromo-5-(trifluoromethyl)-benzonitrile (5.0 g, 20 mmol) and AcOH (22 mL) to give a homogeneous solution. H_2O (22 mL) was added, and the benzonitrile oiled out to provide a biphasic mixture. Conc. H_2SO_4 (22 mL) was added, and the mixture was stirred at 120 °C for 1 h and then at reflux for an additional 5 h. The mixture was cooled to 23 °C and basified to pH 14 in an ice bath with KOH (aq) followed by NaOH (s). A significant exotherm was observed during this process. H_2O was added to dissolve all solids, and the aqueous solution was washed with EtOAc (2 x 200 mL). After acidification to pH 1 with conc. HCl, the resulting biphasic mixture was extracted with EtOAc (3 x 200 mL). The combined organic layers were washed with brine (3 x 200 mL) and dried over $MgSO_4$. Solvent was removed under reduced pressure, and the residue was azeotroped with heptane (4x) to remove any remaining H_2O. Residual solvent was then removed under high vacuum to provide 2-bromo-5-(trifluoromethyl)-benzoic acid (**S3**)[16] (4.42 g, 82%) as a white powder. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, J = 2.0 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.64 (dd, J = 8.1, 2.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.6, 135.7, 131.0, 130.1 (q, J_F = 33.9 Hz), 129.9 (q, J_F = 3.5 Hz), 129.4 (q, J_F = 3.8 Hz), 126.7 (q, J_F = 1.4 Hz), 123.2 (q, J_F = 272.5 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –63.3; IR (neat film, NaCl) ν 3454, 2957, 2925, 2872, 2853, 1664, 1618, 1586, 1513, 1464, 1444, 1419, 1376, 1365, 1342, 1301, 1248, 1220, 1171, 1138, 1092, 1072, 1039, 1018, 1010, 961, 908, 874, 861, 819, 745, 686, 666 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_8H_4F_3BrO_2$ [M]$^+$: 267.9347, found 267.9334.

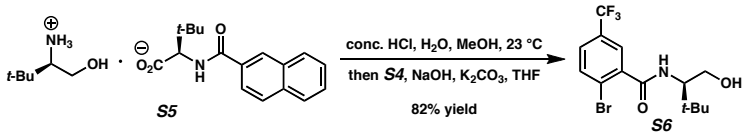


S3 *S4*

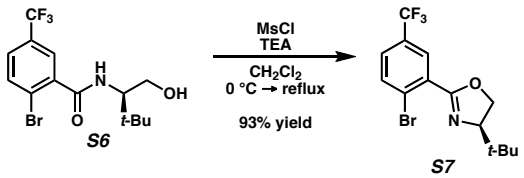
2-Bromo-5-(trifluoromethyl)-benzoyl chloride (S4). A 50 mL round-bottomed flask equipped with a stir bar was charged with 2-bromo-5-(trifluoromethyl)-benzoic acid (**S3**) (1.719 g, 6.39 mmol), CH_2Cl_2 (13 mL), oxalyl chloride (1.1 mL, 13.0 mmol), and DMF (40 μL, 0.517 mmol). A drying tube was attached to the flask, and the reaction was stirred for 25 h at 23 °C. Solvent was removed under reduced pressure, and the residue

(15) Tagawa, H.; Kubo, S. *Chem. Pharm. Bull.* **1984**, *32*, 3047–3052.
(16) Mongin, F.; Desponds, O.; Schlosser, M. *Tetrahedron Lett.* **1996**, *37*, 2767–2770.

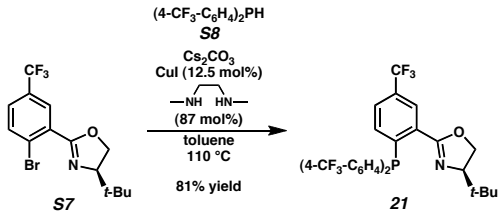
was suspended in hexanes and filtered to remove a precipitate. Solvent was removed under reduced pressure. The crude product was then distilled under high vacuum to provide 2-bromo-5-(trifluoromethyl)-benzoyl chloride (**S4**) as a colorless liquid (1.787 g, 97%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 2.0 Hz, 1H), 7.88 (d, J = 8.3 Hz, 1H), 7.65–7.70 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1, 135.8, 135.7, 130.5 (q, J_F = 3.4 Hz), 130.4 (q, J_F = 34.1 Hz), 129.7 (q, J_F = 3.8 Hz), 125.3 (q, J_F = 1.2 Hz), 122.9 (q, J_F = 272.8 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –63.4; IR ($CHCl_3$, KBr) ν 1775, 1607, 1572, 1469, 1401, 1330 cm^{-1}; HRMS (EI+) m/z calcd. for $C_8H_3ClF_3O$ $[M]^+$: 285.9008, found 285.9002.



Amide S6.[1] Salt **S5**[3] (99% ee, 4.94 g, 12.3 mmol) was suspended in H_2O (32 mL) and MeOH (16 mL). Conc. HCl (5.5 mL) was added, and the mixture was stirred for several minutes. The mixture was then filtered through a Büchner funnel into a round-bottomed flask equipped with a stir bar, washing with H_2O (45 mL). The aqueous solution was basified to pH 10 with NaOH (s), and K_2CO_3 (1.87 g, 13.5 mmol) and THF (30 mL) were added sequentially. 2-Bromo-5-(trifluoromethyl)-benzoyl chloride (**S4**) (88.3% pure by mass (contained 11.7% benzene by mass), 3.991 g, 12.3 mmol) was added, washing the original flask with THF (2 x 3 mL). The reaction mixture turned opaque, and an exotherm was observed. The mixture was stirred for 19 h at 23 °C, at which point it was extracted with Et_2O (3 x 100 mL). The combined organic layers were washed with 10% HCl (aq) (100 mL) and brine (2 x 150 mL). After drying over $MgSO_4$, solvent was removed under reduced pressure. The crude product was then recrystallized from EtOAc (17 mL)/hexanes (86.5 mL) at reflux to provide amide **S6** (3.68 g, 82%) as fine white needles. Observed >99% ee as determined by chiral HPLC analysis (Chiralpak® AD, 5% *i*-PrOH/hexanes, 1 mL/min, 220 nm, t_R (major) = 8.8 min; the minor enantiomer was not observed). A scalemic mixture afforded retention times of 6.6 and 8.9 min for the two enantiomers. $[\alpha]^{24}_D$ –11.78° (99.5% ee material, c 0.495, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 2.2 Hz, 1H), 7.75 (d, J = 8.3 Hz, 1H), 7.52–7.56 (m, 1H), 6.19 (br d, J = 8.6 Hz, 1H), 4.09 (ddd, J = 9.4, 7.3, 3.5 Hz, 1H), 3.98 (ddd, J = 11.2, 5.9, 3.5 Hz, 1H), 3.73 (ddd, J = 11.5, 7.3, 5.5 Hz, 1H), 1.99 (dd, J = 5.7, 5.7 Hz, 1H), 1.06 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 138.7, 134.0, 130.3 (q, J_F = 33.6 Hz), 127.8 (q, J_F = 3.5 Hz), 126.7 (q, J_F = 3.8 Hz), 123.0 (q, J_F = 1.6 Hz), 123.3 (q, J_F = 272.5 Hz), 62.7, 60.2, 33.9, 27.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ –63.2; IR (neat film, NaCl) ν 3410, 3278, 3076, 2965, 2910, 2874, 1644, 1608, 1581, 1548, 1472, 1401, 1368, 1349, 1330, 1300, 1277, 1262, 1173, 1131, 1080, 1050, 1034, 1021, 999, 946, 908, 828, 796, 772, 733, 703, 668, 648 cm^{-1}; HRMS (FAB+) m/z calcd. for $C_{14}H_{18}BrNO_2F_3$ $[M + H]^+$: 368.0473, found 368.0487.

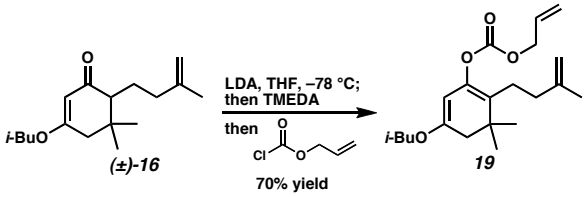


Oxazoline S7.[1] To a flame-dried 250 mL round-bottomed flask equipped with a magnetic stir bar and an oven-dried condenser was added amide **S6** (3.67 g, 9.97 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous CH_2Cl_2 (40 mL) and triethylamine (4.2 mL, 30.1 mmol) were added via syringe, and the reaction was cooled to 0 °C in an ice bath. Methanesulfonyl chloride (0.85 mL, 11.0 mmol) was added via syringe, and the reaction was stirred at 0 °C for 5 min. The reaction was then heated at reflux for 6 h, at which point additional CH_2Cl_2 (15 mL) was added to maintain the appropriate solvent volume. After stirring an additional 18 h at reflux, the reaction was cooled to 23 °C. The reaction was washed with H_2O (50 mL), and the aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were washed with brine (150 mL) and dried over $MgSO_4$. Solvent was removed under reduced pressure. Flash chromatography over silica gel (10 x 5 cm, 7.5% Et_2O/petroleum ether eluent) then provided oxazoline **S7**[1] (3.244 g, 93%) as a colorless viscous liquid. R_f 0.37 (7.5% Et_2O/petroleum ether eluent); $[\alpha]^{24}_D$ +68.01° (*c* 1.035, $CHCl_3$); lit.[1] $[\alpha]^{25}_D$ –64.4° (*c* 1.08, $CHCl_3$, *S* enantiomer); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 2.2 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 1H), 7.49–7.54 (m, 1H), 4.41 (dd, *J* = 10.3, 8.8 Hz, 1H), 4.28 (dd, *J* = 8.4, 8.4 Hz, 1H), 4.14 (dd, *J* = 10.3, 8.1 Hz, 1H), 1.01 (s, 9H).



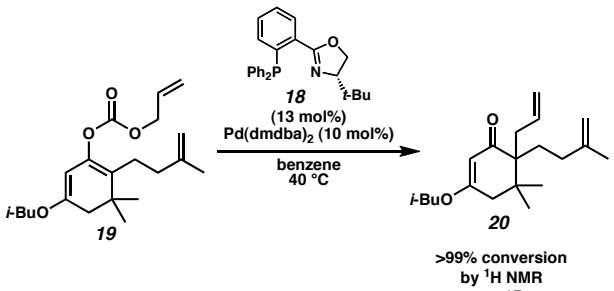
Phosphinooxazoline ligand 21.[1] To a flame-dried 250 mL round-bottomed Schlenck flask equipped with a magnetic stir bar and a septum was added copper(I) iodide (64.4 mg, 0.338 mmol). After sealing with a septum, the flask was wrapped in aluminum foil, placed under high vacuum, and refilled with Ar. Anhydrous toluene (11 mL), *N,N′*-dimethylethylene diamine (0.25 mL, 2.35 mmol), and phosphine **S8** (1.35 g, 4.19 mmol) were added sequentially via syringe, and the reaction was stirred at 23 °C for 30 min. Oxazoline **S7** (944 mg, 2.70 mmol) in anhydrous toluene (3 mL) was then added via syringe, washing the original flask with anhydrous toluene (2 x 4 mL). The flask was opened under positive Ar pressure, and Cs_2CO_3 (3.29 g, 10.1 mmol) was added. The flask was flushed with Ar and sealed with the stopcock, and the reaction was heated to 110 °C for 16.3 h. After cooling to 23 °C, the reaction was filtered through a pad of silica gel, eluting with CH_2Cl_2. Solvent was removed under reduced pressure. Flash chromatography over silica gel (18 x 2.5 cm, 1% Et_2O/pentane eluent) then provided phosphinooxazoline **21**[1] (1.17 g, 81%) as a white powder. R_f 0.087 (1% Et_2O/petroleum ether eluent); $[\alpha]^{24}_D$ +15.04° (*c* 0.495, $CHCl_3$); lit.[1] $[\alpha]^{24}_D$ –16.0° (*c* 2.56, $CHCl_3$, *S* enantiomer); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23–8.27 (m, 1H), 7.54–7.62 (m, 5H), 7.27–7.37 (m, 4H), 6.95 (dd, *J* = 8.2, 3.3 Hz, 1H), 4.24 (dd, *J* = 10.3, 8.6 Hz, 1H), 4.09 (dd, *J* = 8.5, 8.5 Hz, 1H), 3.94 (dd, *J* = 10.1, 8.7 Hz, 1H), 0.68 (s, 9H).

Procedures for Decarboxylative Allylation Mechanistic Experiments



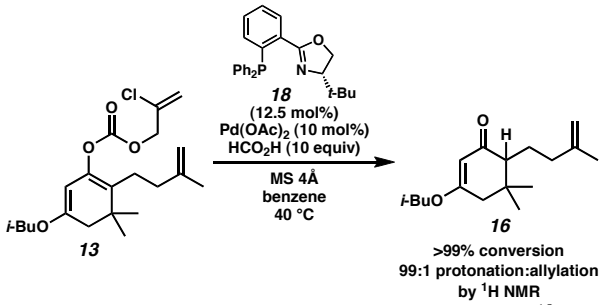
Enol carbonate 19. A 250 mL two-neck round-bottomed flask equipped with a 50 mL addition funnel, a stir bar, and two septa was flame dried under vacuum. After refilling with Ar, anhydrous THF (40 mL) and anhydrous diisopropylamine (1.45 mL, 10.3 mmol) were added via syringe, and the solution was cooled to 0 °C in an ice bath. *n*-BuLi (2.51 M in hexanes, 3.8 mL, 9.54 mmol) was added dropwise via the addition funnel over 22 min, washing the funnel sequentially with anhydrous hexanes (5 mL) and anhydrous THF (5 mL) upon complete addition. The reaction was then stirred at 0 °C for 30 min. The resulting LDA solution was cooled to –78 °C over 30 min. Olefin (±)-**16** (2.285 g, 8.64 mmol) in anhydrous THF (10 mL) was then added dropwise over 11 min via the addition funnel, washing the funnel with anhydrous THF (5 mL) upon complete addition. A yellow solution was obtained. After stirring at –78 °C for 1 h, *N,N,N′,N′*-tetramethylethylenediamine (1.55 mL, 10.3 mmol) was added dropwise quickly via syringe. After stirring at –78 °C for an additional 1 h, allyl chloroformate (1.0 mL, 9.41 mmol) in anhydrous THF (10 mL) was then added dropwise over 21 min via the addition funnel, washing the funnel with THF (5 mL) upon complete addition. The reaction was stirred for an additional 3 h at –78 °C, at which time saturated $NaHCO_3$ (aq) (35 mL) and H_2O (35 mL) were added. The mixture was allowed to warm to 23 °C with the aid of a 23 °C water bath, at which time the organic layer was immediately separated. The aqueous layer was extracted with Et_2O (2 x 200 mL), and the combined organic layers were washed with brine (2 x 200 mL) and dried over $MgSO_4$. Solvent was removed under reduced pressure. Flash chromatography over Florisil® (100-200 mesh, 12.5 x 5 cm, 2.5% Et_2O/petroleum ether eluent) then provided enol carbonate **19** (2.101 g, 70%) as a slightly pale yellow liquid containing residual Et_2O (<1% by mass) and minor unidentified impurities (5% by area) by ^{1}H NMR spectroscopy. R_f 0.21 (2.5% Et_2O/petroleum ether eluent); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.96 (ddt, J = 17.1, 10.5, 5.7 Hz, 1H), 5.39 (ddt, J = 7.1, 1.5, 1.5 Hz, 1H), 5.28 (ddt, J = 10.5, 1.2, 1.2 Hz, 1H), 4.76 (s, 1H), 4.66–4.71 (m, 2H), 4.66 (ddd, J = 5.7, 1.4, 1.4 Hz, 2H), 3.47 (d, J = 6.6 Hz, 2H), 2.19 (s, 2H), 2.09–2.17 (m, 2H), 2.01–2.09 (m, 2H), 1.97 (app. septet, J = 6.7 Hz, 1H), 1.74 (br s, 3H), 1.08 (s, 6H), 0.94 (d, J = 6.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 153.5, 146.0, 141.9, 131.5, 123.1, 119.0, 109.7, 91.3, 73.8, 68.6, 43.4, 37.9, 35.4, 27.8, 26.0, 24.1, 22.4, 19.2; IR (neat film, NaCl) ν 2960, 2874, 1758, 1662, 1622, 1470,

1422, 1382, 1363, 1330, 1292, 1241, 1160, 1146, 1109, 1041, 1024, 994, 970, 952, 887, 784 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{21}H_{32}O_4$ $[M]^+$: 348.2301, found 348.2307.



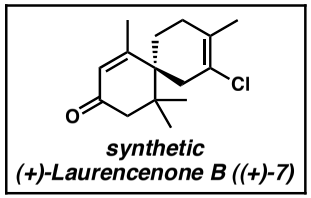
Decarboxylative allylation of enol carbonate 19.[17] To a flame-dried 1 dram screw-cap vial equipped with a stir bar and a septum-bearing cap was added bis(3,5,3′,5′-dimethoxydibenzylideneacetone)palladium(0) (4.0 mg, 0.00491 mmol) and phosphinooxazoline ligand **18** (2.5 mg, 0.00645 mmol). After sealing with the septum cap, the vial was placed under high vacuum and refilled with Ar. Anhydrous benzene (0.75 mL) was added via syringe, and the resulting solution was stirred for 29 min at 23 °C. Concurrently, a second flame-dried 1 dram screw-cap vial equipped with a septum-bearing cap was charged with enol carbonate **19** (99.5% pure by mass (contained 0.5% Et_2O by mass), 17.5 mg, 0.050 mmol), and the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (0.75 mL) was added via syringe, and the resulting solution was transferred to the catalyst solution via syringe. The reaction was transferred to a 40 °C heating block and stirred at 40 °C for 1 h. After cooling to 23 °C, the reaction was filtered through a plug of silica gel in a pipette, eluting with Et_2O. Solvent was removed under reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture revealed >99% conversion and ≥99% α,ω-diene **20**. R_f 0.07 (5% Et_2O/petroleum ether eluent); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85–6.04 (br m, 1H), 5.24 (d, J = 0.97 Hz, 1H), 5.03–5.10 (m, 1H), 4.96–5.01 (m, 1H), 4.65–4.69 (m, 1H), 4.64 (br s, 1H), 3.58 (dd, J = 9.5, 6.6 Hz, 1H), 3.54 (dd, J = 9.3, 6.8 Hz, 1H), 2.35–2.90 (br m, 2H), 2.28 (dd, J = 15.4, 8.1 Hz, 1H), 1.94–2.10 (br m, 2H), 2.01 (app. septet, J = 6.7 Hz, 1H), 1.62–1.89 (br m, 3H), 1.69 (s, 3H), 1.10 (s, 3H), 1.07 (s, 3H), 0.96 (d, J = 6.8, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.2, 173.0, 146.5, 137.1 (br), 116.1, 109.3, 100.7, 74.5, 53.5, 42.7, 38.7, 33.7 (br), 32.8, 28.7, 27.7, 25.5, 25.3, 22.8, 19.1; IR (neat film, NaCl) ν 3072, 2961, 2937, 2876, 1653, 1621, 1471, 1449, 1405, 1383, 1366, 1297, 1221, 1207, 1172, 1149, 1009, 995, 967, 955, 907, 885, 846, 833, 768, 755, 654 cm^{-1}; HRMS (EI+) *m/z* calcd. for $C_{20}H_{32}O_2$ $[M]^+$: 304.2402, found 304.2388.

(17) Behenna, D. C.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 15044–15045.



Decarboxylative protonation of enol carbonate 13.[18] A flame-dried 1 dram screw-cap vial equipped with a stir bar and a septum-bearing cap was charged with powdered activated 4 Å molecular sieves (119 mg). The vial was placed under high vacuum, the sieves were flame-dried, and the vial was refilled with Ar. This was repeated for a total of three cycles. After cooling to 23 °C, $Pd(OAc)_2$ (1.1 mg, 0.0049 mmol) and phosphinooxazoline ligand **18** (2.4 mg, 0.0062 mmol) were added, and the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (0.75 mL) was added via syringe, and the reaction was placed in 40 °C heating block and stirred at 40 °C for 31 min. Concurrently, a second oven-dried 1 dram screw-cap vial equipped with a septum-bearing cap was charged with enol carbonate **13** (19.0 mg, 0.0496 mmol), and the vial was placed under high vacuum and refilled with Ar. Anhydrous benzene (0.75 mL) was added via syringe. To the catalyst solution at 40 °C was then added formic acid (19 μL, 0.504 mmol) followed by the enol carbonate **13** solution via syringe. The reaction was stirred at 40 °C for 3.1 h. After cooling to 23 °C, the reaction was filtered through a plug of silica gel in a pipette, eluting with Et_2O. Solvent was removed under reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture revealed >99% conversion and 99:1 olefin **16**:α,ω-diene **12**.

(18) Mohr, J. T.; Nishimata, T.; Behenna, D. C.; Stoltz, B. M. *J. Am. Chem. Soc*. **2006**, *128*, 11348–11349.



synthetic
(+)-Laurencenone B ((+)-7)

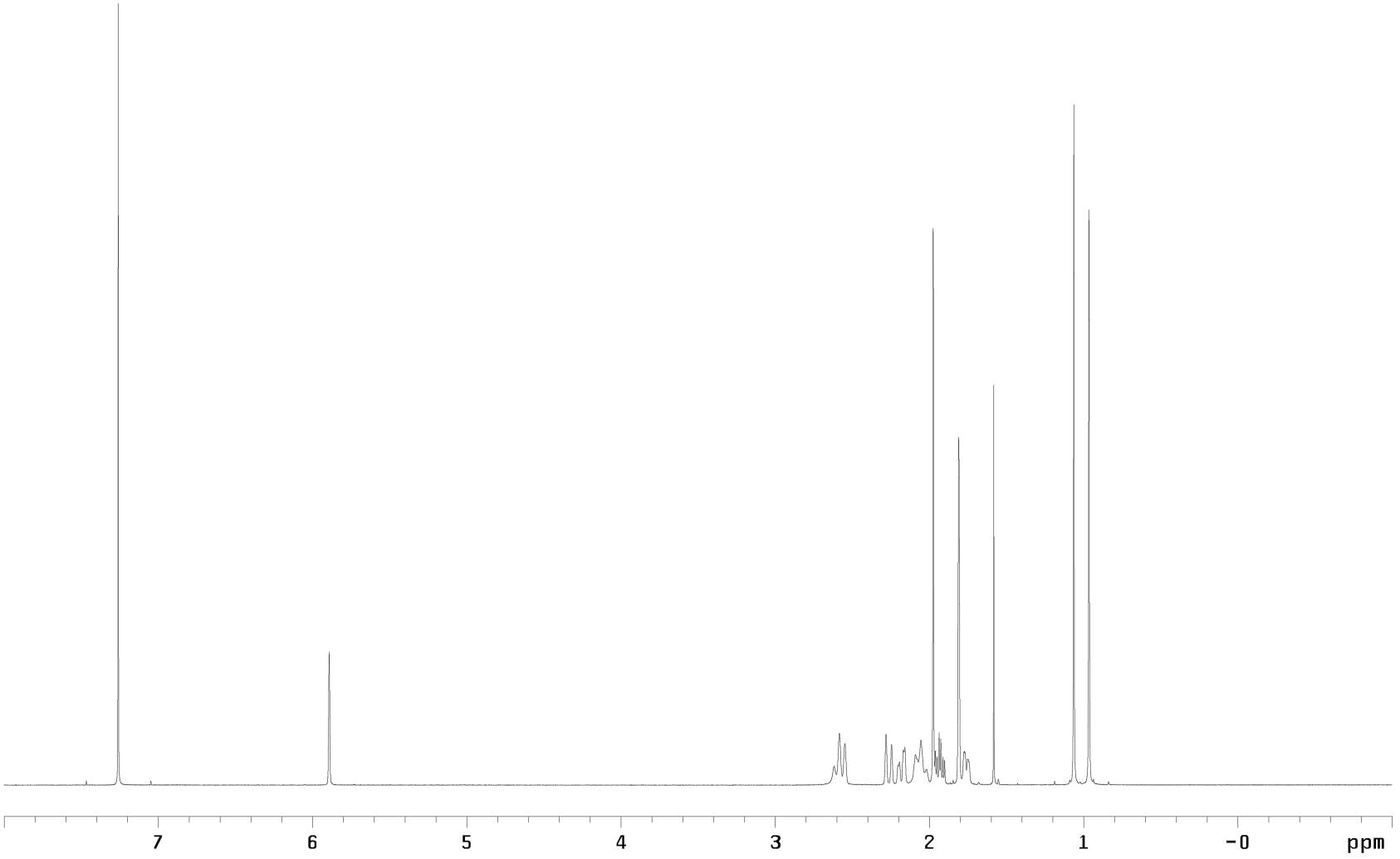
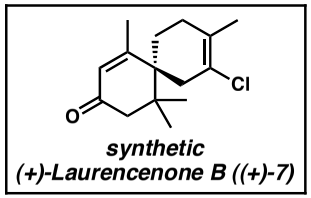


Figure S.1 ^{1}H NMR (500 MHz, $CDCl_3$) of synthetic (+)-laurencenone B ((+)-**7**).



synthetic
(+)-Laurencenone B ((+)-7)

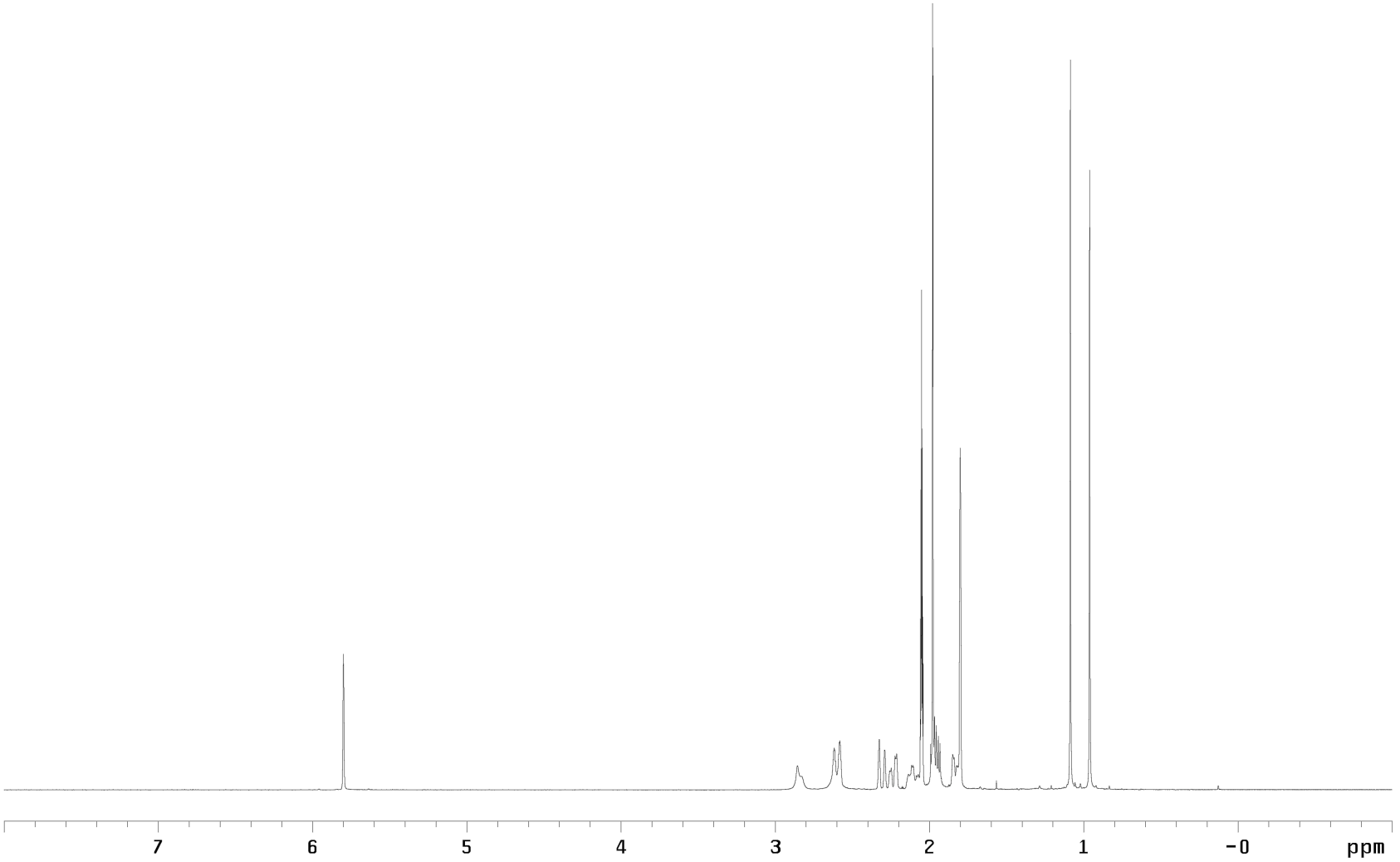


Figure S.2 ^{1}H NMR (500 MHz, acetone-d_6) of synthetic (+)-laurencenone B ((+)-**7**).

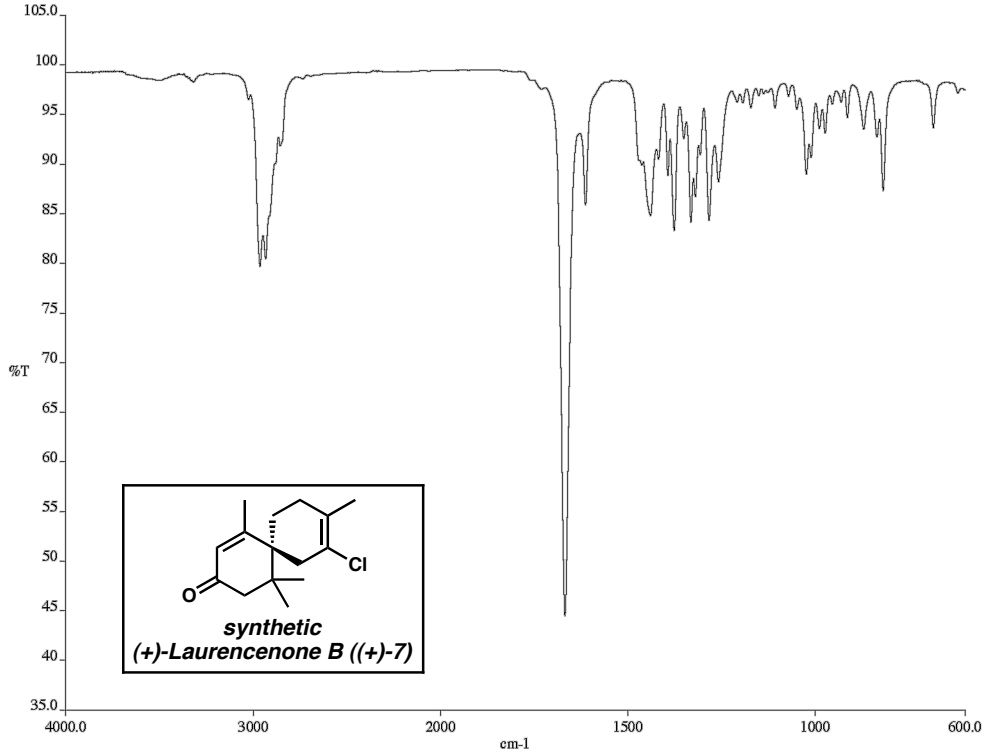


Figure S.3 Infrared spectrum (neat film/NaCl) of synthetic (+)-laurencenone B ((+)-**7**).

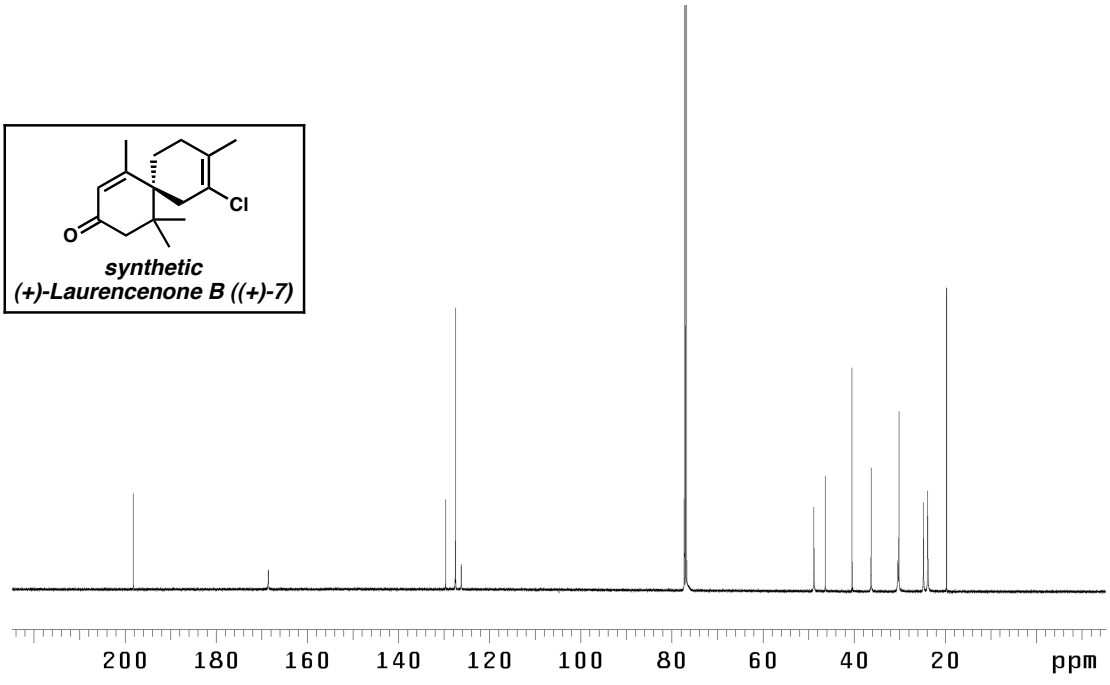


Figure S.4 ^{13}C NMR (126 MHz, $CDCl_3$) of synthetic (+)-laurencenone B ((+)-**7**).

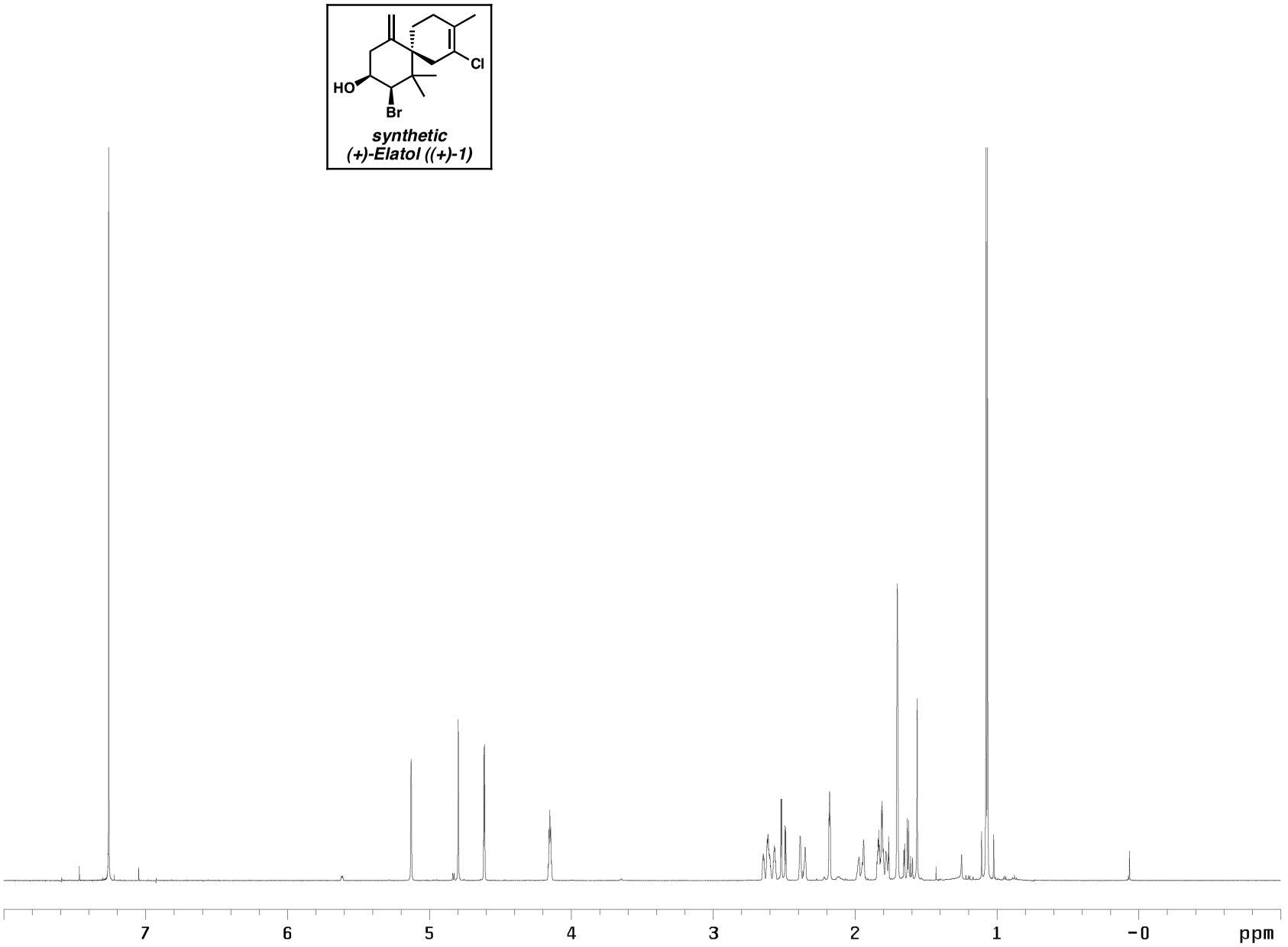


Figure S.5 ^{1}H NMR (500 MHz, $CDCl_3$) of synthetic (+)-elatol ((+)-(**1**)).

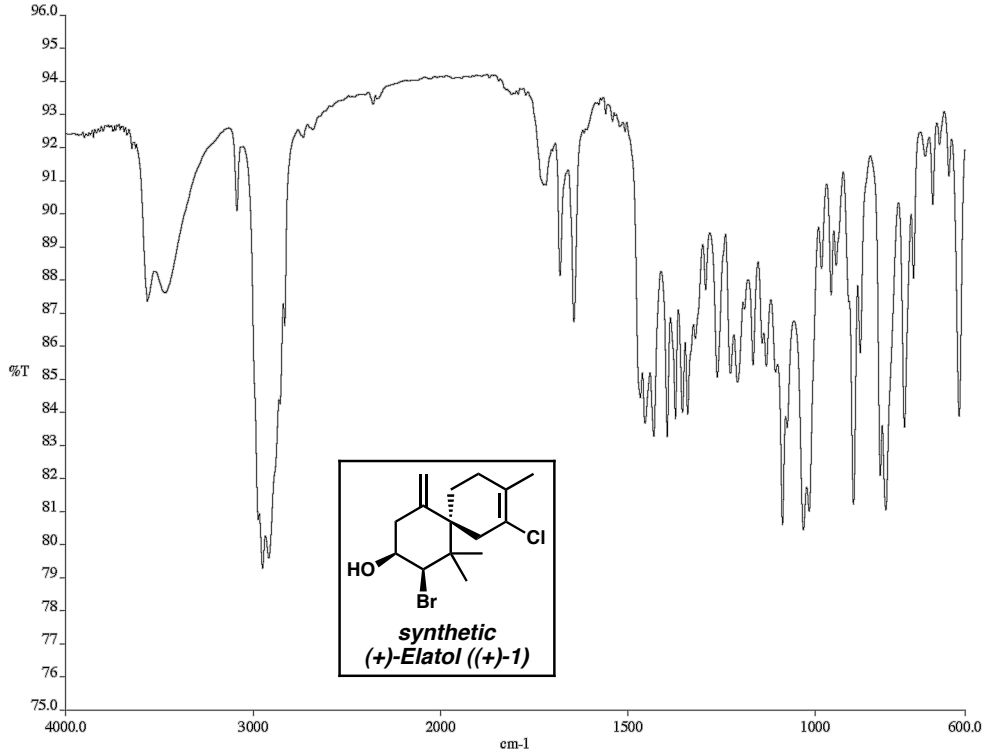


Figure S.6 Infrared spectrum (neat film/NaCl) of synthetic (+)-elatol ((+)-(**1**)).

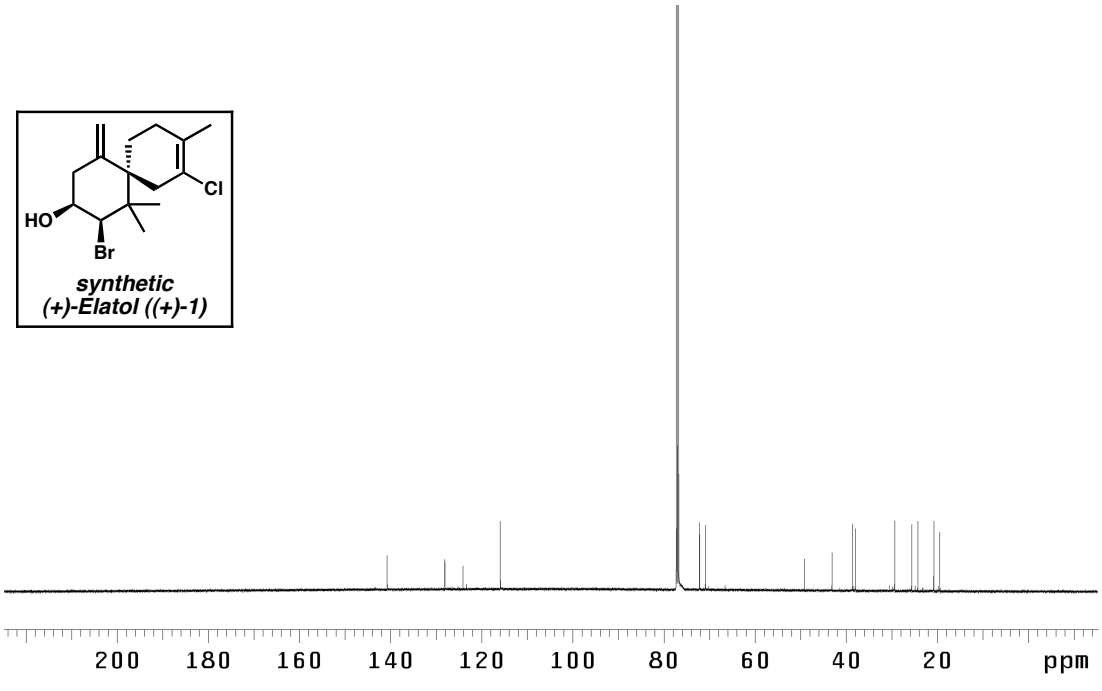
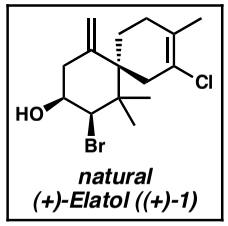


Figure S.7 ^{13}C NMR (126 MHz, $CDCl_3$) of synthetic (+)-elatol ((+)-(**1**)).



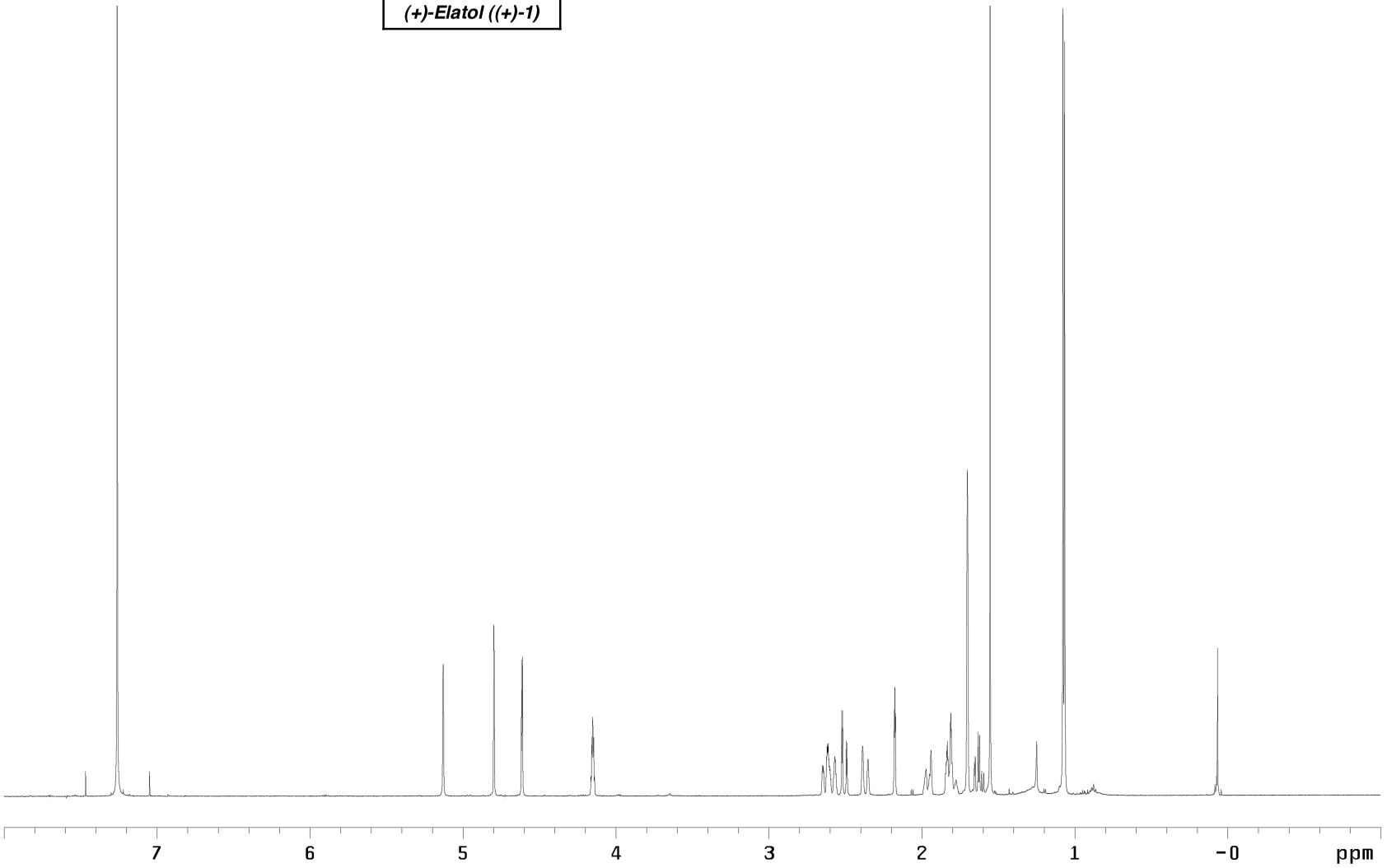


Figure S.8 ^{1}H NMR (500 MHz, $CDCl_3$) of a natural sample of (+)-elatol ((+)-(**1**)).

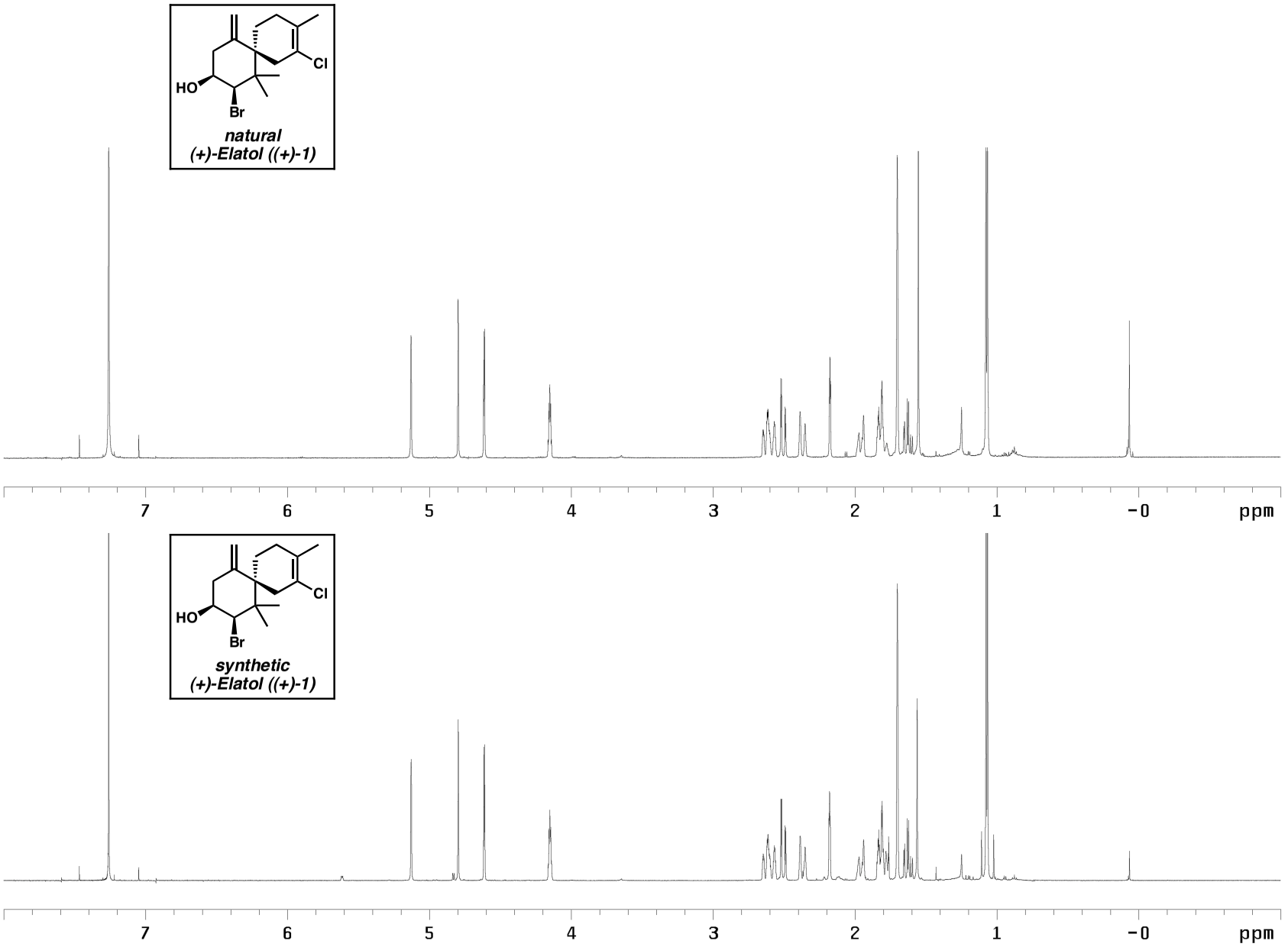


Figure S.9 Overlay of ^{1}H NMR spectra (500 MHz, $CDCl_3$) of natural and synthetic (+)-elatol ((+)-**1**).