Cyclohexenone Annelation by Alkylidene C−H Insertion: Synthesis of Oxo-*T*-cadinol

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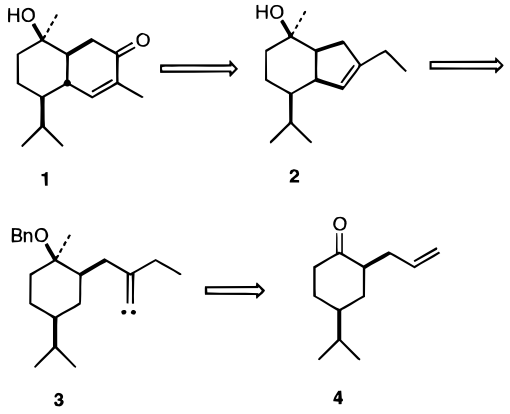
A new procedure for cyclohexenone annelation has been developed. Thus, alkylation of 4-isopropylcyclohexanone with allyl bromide gives, over several steps, ketone **8**. Exposure to (trimethylsilyl)diazomethane and MeLi smoothly cyclized **8** to the cyclopentene **9** by insertion of the intermediate alkylidene carbene into the unactivated methylene CH. On debenzylation, ozonolysis, and subsequent aldol condensation, **9** is transformed into oxo-*T*-cadinol (**1**).

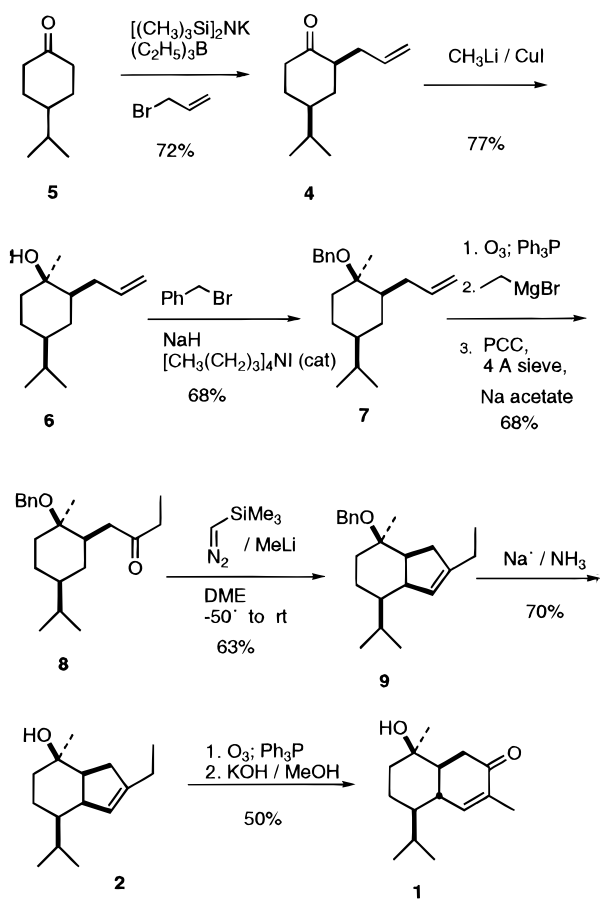
Cyclohexane derivatives are ubiquitous in nature. As a result, many procedures have been developed for constructing six-membered rings. A subset of these procedures may be used to anneal a six-membered ring onto a preexisting ring. Heretofore, such annelations could only be effected if the two atoms to which the new ring was to be attached were first *each* functionalized. Our work and that of others on intramolecular alkylidene insertion[1−3] led us to speculate that an alternative approach might be possible. Thus, a simple allyl group, such as that in **4**, could be homologated to the alkylidenecarbene **3**. Intramolecular CH insertion could then proceed to form **2**. If CH insertion were successful, ozonolysis followed by aldol condensation would give **1**. The net process would convert a pendant allyl group into the fused cyclohexenone.



We now report that the desired CH insertion does indeed proceed smoothly, establishing a new procedure for cyclohexenone annelation. This allows a simple synthesis of oxo-*T*-cadinol (**1**), isolated from scented myrrh (*Commiphora guidottii*).[4] Ketone **1** has recently been shown to have calcium channel antagonist properties.[5] Ketone **1** had not previously been synthesized, although the ketone epimeric at the quaternary center has been prepared by Caine.[6]

The synthesis is outlined in Scheme 1. Starting with commercially available 4-(methylethyl)cyclohexanone (**5**),

Scheme 1



allylation using potassium bis(trimethylsilyl)amide and triethylborane[7] led to a mixture of *cis* and *trans* epimers, which was converted to the more thermodynamically stable *cis* product **4** by refluxing in toluene with a catalytic amount of potassium *tert*-butoxide. The desired *cis* alcohol **6,** requiring an axial addition of methyl anion to **4,** was secured using the procedure of Still and Macdonald.[8] After benzyl protection, the allyl ether was converted to the ketone **8** via ozonolysis to the aldehyde, addition of ethylmagnesium bromide, and finally oxidation using a 1:1:1 mixture of PCC, 4 Å molecular sieve, and sodium acetate.[9]

The key question was whether intramolecular alkylidene insertion into the electronically unreactive and

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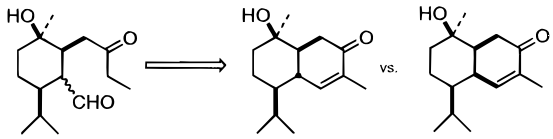
geometrically constrained ring methylene would proceed efficently.[10] In fact, CH insertion proceeded smoothly to give the bicyclononene **9** in 63% yield. Methyllithium in ether provided far better yields than *n*-butyllithium in hexane, and hexane-free (trimethylsilyl)diazomethane was used. As we have previously observed, it was critically important to carry out the cyclization in DME rather than ether or THF.[1]

To complete the synthesis of oxo-*T*-cadinol, **9** was first deprotected under dissolving metal conditions. The resulting bicyclic alcohol **2** was ozonized and the crude aldehyde taken directly to **1** by refluxing with 5% KOH in methanol.[6] The final cyclization produced a product whose TLC, ^{13}C NMR, ^{1}H NMR, IR, and mass spectra were identical to those of authentic material,[11] which has been assigned as the *trans* isomer. Under the equilibrating aldol condensation condition we employed, the cyclization could potentially proceed to give either a *cis* or *trans* fused system. Both isomers were therefore examined for their energy minima. The diastereomers were constructed in the Builder module of InsightII 2.3, and minimization and dynamic simulations were effected in Discover 2.9 using the cff91 forcefield (Biosym Technologies, Inc., San Diego). A modified quenched dynamics[12,13] protocol was used to generate 100 low-energy conformations of each isomer. The lowest energy conformation found for the *cis* isomer had the chair geometry at −12.6 kcal. The lowest energy *trans* isomer had the chair geometry at −13.8 kcal. Assuming constant entropy and solvation enthalpy, this difference in total strain energy represents a free energy difference (ΔG) of −1.2 kcal, which can be converted to an equilibrium constant (K_{eq}) of 7.2 or a ratio of 88:12 *trans* to *cis*. It is interesting to note that the ^{1}H spectra of both the natural material and the synthetic product show a minor absorption at 1.05 ppm, which may represent a methyl group of the *cis* isomer.



The approach outlined here leads to the racemic natural product. The starting ketone **5** is prochiral. If the initial allylation could be effected with enantiocontrol, the new cyclohexenone annelation procedure described here could be used to prepare the enantiomerically pure natural product.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded using a Varian VXR-300S spectrometer at 300 MHz and 75 MHz, respectively. The infrared (IR) spectra were determined as neat oils on a Perkin-Elmer Model 1650 FTIR spectrophotometer. Mass spectra (MS) were obtained using FTMS at an ionizing potential of 70 eV. Substances for which C,H analysis are not reported were purified as specified and gave spectroscopic data consistent with being >95% the assigned structure. R_f values indicated refer to thin layer chromatography on EM Science 5 × 10 cm, 250 μm analytical plates coated with silica gel 60 F_{254} and developed in the solvent indicated. Materials were visualized using ceric molybdate in 50% aqueous methanol as stain. Column chromatography was performed on EM Science silica gel 60, 230−400 mesh. Solvent mixtures are volume/volume mixtures.

(2*S,4*S**)-4-Methylethyl-2-(2-propenyl)cyclohexanone (4).** Allylation was effected by the method of Negishi. Thus, potassium bis(trimethylsilyl)amide (150 mL, 0.5 M in toluene, 75 mmol) was added dropwise to a solution of 4-(methylethyl)cyclohexanone (**5**) (10.0 g, 71.4 mmol) in 100 mL of dry THF. Triethylborane (93.9 mL, 1.0 M in THF, 93.8 mmol) was added, and the mixture was stirred at rt for 15 min. 3-Bromopropene (9.30 mL, 0.11 mol) was added, and the mixture was stirred for 24 h. The mixture was poured into a 1:1 mixture of 1.0 N aqueous NaOH and 30% aqueous H_2O_2 and extracted with ethyl acetate (4 × 200mL) and chloroform (2 × 200 mL). The combined organic extracts were dried (K_2CO_3) and concentrated *in vacuo*, and the residue was chromatographed. Two major fractions were isolated, one containing the *cis* epimer (3.5 g, TLC R_f 0.40) and the other containing a mixture of both the *cis* and *trans* (R_f 0.35) epimers (6.3 g). The mixture of epimers was stirred in toluene (100 mL) with 50 mg of potassium *tert*-butoxide at reflux for 24 h. The reaction was then cooled and poured into water. This was extracted with ethyl acetate (3 × 100 mL) and chloroform (2 × 100 mL). The combined organic extract was dried (K_2CO_3) and concentrated *in vacuo*, and the residue was chromatographed to give 5.8 g of the *cis* product providing a total of 9.3 g (72% yield) of **4** as a thin colorless oil **(4)**: TLC R_f (10% ethyl acetate/hexanes) = 0.40; ^{1}H NMR (δ) 5.83 (m, 1 H), 5.02 (m, 2 H), 2.59 (m, 1 H), 2.38 (m, 3 H), 2.08 (m, 3 H), 1.61 (m, 1 H), 1.43 (dd, J = 5.9, 12.5 Hz, 1 H), 1.12 (q, J = 12.8 Hz, 1 H), 0.92 (d, J = 2.2 Hz, 3 H), 0.90 (d, J = 2.2 Hz, 3 H); ^{13}C NMR (δ) C=O, 214.0, CH, 138.0, 49.8, 43.8, 32.1, CH_2, 117.5, 41.3, 36.5, 30.9, 26.0, CH_3, 20.0; IR (cm^{-1}) 2958, 2870, 1714, 1640, 1466, 1444, 1432; MS (*m*/*z*) 180 (84), 165 (21), 153 (15), 136 (100), 121 (37); HRMS calcd for $C_{12}H_{20}O$ 180.151 415, found 180.151 466.

(1*R,2*S**,4*S**)-1-Methyl-4-(methylethyl)-2-(2-propenyl)-cyclohexanol (6).** Methyllithium (62.9 mL, 1.4 M in ether, 88.8 mmol) was added to a solution of copper(I) iodide (6.34 g, 33.3 mmol) in ether (100 mL) at 0 °C. The mixture was stirred for 10 min before being cooled further to −70 °C. Ketone **4** (2.0 g, 11.1 mmol) in 10 mL of dry ether was added dropwise, and the mixture was stirred for 20 min while the temperature

(3) For other leading references to cyclopentene construction by intramolecular C−H insertion by an alkylidene carbene, see: (a) Gilbert, J. C.; Giamalva, D. H.; Weerasooriya, U. *J. Org. Chem.* **1983**, *48*, 5251. (b) Gilbert, J. C.; Giamalva, D. H.; Baze, M. E. *J. Org. Chem.* **1985**, *50*, 2557. (c) Ochiai, M.; Uemura, K.; Masaki, Y. *J. Am. Chem. Soc.* **1993**, *115*, 2528. (d) Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta* **1979**, *62*, 852. (e) Ohira, S.; Okai, K.; Moritani, T. *J. Chem. Soc., Chem. Commun.* **1992**, 721. (f) Baird, M. S.; Baxter, A. G. W.; Hoorfar, A.; Jeffries, I. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2575. (g) Tykwinski, R. R.; Stang, P. J.; Persky, N. E. *Tetrahedron Lett.* **1994**, *35*, 23. (h) Kunishima, M.; Hioki, K.; Tani, S.; Kato, A. *Tetrahedron Lett.* **1994**, *35*, 7523. (i) Kim, S.; Cho, C. M.*Tetrahedron Lett.* **1994**, *35*, 8405. (j) Ohira, S.; Sawamoto, T.; Yamato, M. *Tetrahedron Lett.* **1995**, *36*, 1537. (k) Schildknegt, K.; Bohnstedt, A. C.; Feldman, K. S.; Sambandam, A. *J. Am. Chem. Soc.* **1995**, *117*, 7544.

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(5) Zygmunt, P. M.; Larsson, B.; Sterner, O.; Vinge, E.; Hogestatt, E. D. *Pharmacol. Toxicol.* **1993**, *73*, 3.

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(7) Negishi, E.; Idacavage, M. J.; DiPasquale, F.; Silveira, A. *Tetrahedron Lett.* **1979**, 845.

(8) Macdonald, T. L.; Still, W. C. *J. Am. Chem. Soc.* **1975**, *97*, 5280.

(9) (a) Corey, E. J; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647. (b) Maloney, J. R.; Lyle, R. E.; Saavedra, J. E.; Lyle, G. G. *Synthesis* **1978**, 212. (c) Herscovici, J.; Antonakis, K. *J. Chem. Soc., Chem. Commun.* **1980**, 561.

(10) While this work was in progress, a report (ref 3h) of such an alkylidene insertion appeared.

(11) The ^{1}H spectrum of the natural product was kindly provided by P. M. Zygmunt.

(12) O'Conner, S. D.; Smith, P. E.; Al-Obeidi, F.; Pettitt, B. M. *J. Med. Chem.* **1992**, *35*, 2870.

(13) Simulation conditions: 1 fs timestep, dielectric constant ϵ = 80, temperature = 2500 °C, minimize every ps using, in sequence, steepest descent (200 steps or RMSD < 1.00 kcal/A), conjugate gradient (500 steps or RMSD < 0.1 kcal/A), and quasi-Newton−Raphson (1000 steps or RMSD < 0.01 kcal/A). The total simulation time of 100 ps requires a total cpu time of 22 h 55 min running in parallel on four R8000 Silicon Graphics processors. The input files are available as supporting information.

was maintained at −70 °C. The reaction was poured into saturated aqueous ammonium chloride, and an additional 200 mL of ether was added. The layers were separated, and the aqueous layer was extracted with ether (4 × 100 mL). The organic fractions were combined, passed through a pad of Celite, and then dried (K_2CO_3). The solvent was removed *in vacuo*, and the residue was chromatographed to give 1.68 g (77% yield) of **6** as a colorless oil: TLC R_f (10% ethyl acetate/hexanes) = 0.35; ^{1}H NMR (δ) 5.82 (m, 1 H), 5.05 (m, 2 H), 2.41 (m, 1 H), 1.92 (m, 1 H), 1.25−1.72 (m, 7 H), 1.23 (s, 3 H), 1.02 (m, 2 H), 0.87 (d, J = 2.6 Hz, 3 H), 0.85 (d, J = 2.6 Hz, 3 H); ^{13}C NMR (δ) COH, 71.2, CH, 138.3, 45.5, 43.9, CH_2, 115.7, 40.9, 34.7, 30.7, 24.8, CH_3, 28.62 19.9, 19.7; IR (cm^{-1}) 3478 (broad), 2956, 2932, 1640, 1464, 1440. Anal. Calcd for $C_{13}H_{24}O$: C, 79.59; H, 12.24; O, 8.16. Found: C, 79.45; H, 12.35; O, 7.95.

(1*R,2*S**,4*S**)-1-Methyl-4-(methylethyl)-1-(phenylmethoxy)-2-(2-propenyl)cyclohexane (7).** Alcohol **6** (8.44 g, 43.1 mmol in 50 mL of dry THF) was added to a stirring solution of NaH (2.58 g, 64.6 mmol, 60% dispersion in mineral oil, washed twice with hexanes) in THF (200 mL), and the mixture was stirred at rt for 20 min. Tetrabutylammonium iodide (1.59 g, 4.3 mmol) was added to the reaction mixture followed by α-bromotoluene (11.1 g, 64.6 mmol). The reaction was heated at reflux for 24 h. After being cooled to rt, it was poured into water and extracted with ethyl acetate (4 × 400 mL) and chloroform (2 × 200 mL). The organic fractions were combined and then dried (K_2CO_3) and concentrated *in vacuo*. The residue was chromatographed to give 8.38 g (68% yield) of **7** as a colorless oil: TLC R_f (2% ethyl acetate/hexanes) = 0.75; ^{1}H NMR (δ) 7.35 (m, 4 H), 7.25 (m, 1 H), 5.80 (m, 1 H), 5.00 (m, 2 H), 4.40 (d, J = 11.7 Hz, 1 H), 4.34 (d, J = 11.7, 1 H), 2.49 (m, 1 H), 2.09 (m, 2 H), 1.54 (m, 1 H), 1.27−1.50 (m, 3 H), 1.24 (s, 3 H), 1.02−1.20 (m, 3 H), 0.87 (d, J = 3.7 Hz, 3 H), 0.84 (d, J = 3.3 Hz, 3 H); ^{13}C NMR (δ) C, 140.6, CO, 74.7, CH, 139.2, 128.1, 126.7, 47.6, 44.0, 32.9, CH_2, 115.0, 62.3, 35.0, 34.5, 30.4, 24.9, CH_3, 23.6, 20.0, 19.7; IR (neat, cm^{-1}) 2956, 2934, 2868, 1640, 1466, 1452, 1384, 1368, 1090, 1064. Anal. Calcd for $C_{20}H_{30}O$: C, 83.92; H, 10.49. Found: C, 83.75; H, 10.30.

(1*R,2*R**,4*S**)-1-Methyl-4-(methylethyl)-1-(phenylmethoxy)-2-(2-oxobutyl)cyclohexane (8).** Ether **7** (5.04 g, 17.6 mmol) and 15 mg of Sudan III were placed in 150 mL of methylene chloride and chilled to −78 °C. Ozone was passed through the reaction solution until the red Sudan III color faded. Nitrogen was passed through the reaction for 10 min, and then triphenylphosphine (5.55 g, 21.2 mmol) was added. The mixture was allowed to warm to rt and stir for 3 h. The solvent was stripped *in vacuo*, and the residue was chromatographed, giving the aldehyde (4.21 g, 83% yield) as a colorless oil: TLC R_f (10% ethyl acetate/hexanes) = 0.45; ^{1}H NMR (δ) 9.80 (s, 1 H), 7.30 (s, 4 H), 7.22 (m, 1 H), 4.35 (dd, J = 11.5, 11.5 Hz, 2 H), 2.65 (m, 1 H), 2.45 (m, 1 H), 2.15 (m, 1 H), 1.95 (m, 1 H), 1.39 (m, 4 H), 1.23 (m, 3 H), 1.20 (s, 3 H), 1.18 (m, 1 H), 0.85 (d, J = 1.5 Hz, 3 H), 0.83 (d, J = 1.5 Hz, 3 H); ^{13}C NMR (δ) C, 139.9, CO, 74.4, CH, 128.2, 126.9, 43.9, 42.7, 32.7, CH_2, 62.5, 45.7, 34.4, 31.9, 24.6, CH_3, 23.6, 19.9, 19.7; IR (neat, cm^{-1}) 2956, 2932, 1722, 1498, 1452, 1384, 1090, 1062.

To a 0 °C solution of the aldehyde (2.68 g, 9.3 mmol) in 100 mL of methylene chloride was added 14.0 mL of ethylmagnesium bromide (1.0 M in THF, 14.0 mmol) over 10 min. The mixture was allowed to stir for 1 h at 0 °C and then was warmed to rt and stirred for 3 h. The mixture was then poured into a saturated aqueous solution of ammonium chloride, and an additional 200 mL of methylene chloride was added. The layers were separated, and the aqueous layer was extracted with methylene chloride (4 × 200 mL). The organic fractions were combined and then dried (K_2CO_3) and concentrated *in vacuo*. The residue was chromatographed, giving 2.82 g (95% yield) of the secondary alcohol as a colorless oil. The desired alcohol was isolated as a mixture of diastereomers: TLC R_f (20% ethyl acetate/hexanes) = 0.50.

Oxidation of the alcohol (2.62 g, 8.24 mmol) was accomplished using a 1:1:1 by weight mixture of PCC, sodium acetate, and 4 Å sieves (3.56 g, finely ground) in 100 mL of methylene chloride. The mixture was allowed to stir at rt for 3 h, after which time 200 mL of ether was added and the solution was filtered through Celite. The solvent was concentrated *in vacuo*, and the resulting residue was chromatographed to give 2.24 g of ketone **8** (68% overall yield from ether **7**) as a colorless oil: TLC R_f (10% ethyl acetate/hexanes) = 0.57; ^{1}H NMR (δ) 7.40 (d, J = 4.4 Hz, 4 H), 7.35 (m, 1 H), 4.47 (d, J = 11.7, 1 H), 4.43 (d, J = 11.7, 1 H), 2.86 (dd, J = 3.7, 13.6 Hz, 1 H), 2.50 (m, 3 H), 2.20 (m, 1 H), 2.10 (m, 1 H), 1.27−1.60 (m, 7 H), 1.34 (t, J = 7.3 Hz, 3 H), 1.25 (s, 3 H), 0.94 (d, J = 5.5 Hz, 6 H); ^{13}C NMR (δ) CO, 212.2, C, 140.3, CH, 128.2, 126.8, 43.6, 42.8, 32.7, CO, 74.4, CH_2, 62.3, 43.7, 36.8, 34.5, 31.9, 24.5, CH_3, 23.5, 20.0 19.6, 7.9; IR (neat, cm^{-1}) 2958, 2934, 1714, 1452, 1368; HRMS calcd for $C_{21}H_{32}O_2$ 316.240 231, found 316.239 435.

(1*S,2*R**,5*R**,6*R**)-8-Ethyl-2-methyl-5-(methylethyl)-2-(phenylmethoxy)bicyclo[4.3.0.]non-7-ene (9).** Methyllithium (4.6 mL, 1.4 M in diethyl ether, 6.0 mmol) was added slowly to a solution of hexane-free (trimethylsilyl)diazomethane (915 mg, 8.0 mmol) in 50 mL of DME at −78 °C. The cooling bath was removed, and the heterogeneous mixture was allowed to warm until it became clear amber (approximately −30 °C). The mixture was chilled to −50 °C, and then ketone **8** (633 mg, 2.0 mmol) in 5 mL of DME was added dropwise over 5 min. The mixture was stirred at −50 °C for 1 h and then was allowed to come to rt over 3 h. Saturated aqueous ammonium chloride (50 mL) was then added, and the mixture was allowed to stir for 10 min. An additional 50 mL of water was added to the mixture, which was then extracted with ethyl acetate (4 × 200 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was chromatographed to give **9** (394 mg, 63% yield) as a colorless oil: TLC R_f (5% ethyl acetate in hexanes) = 0.75 ; ^{1}H NMR (δ) 7.29−7.39 (m, 4 H), 7.20 (m, 1 H), 5.50 (s, 1 H), 4.42 (s, 2 H), 2.7 (bt, 1 H), 2.34 (bt, 1 H), 2.0−2.15 (m, 4 H), 1.95 (m, 1 H), 1.65 (m, 1 H), 1.4 (m, 1 H), 1.29 (m, 1 H), 1.24 (s, 3 H), 1.15 (m, 2 H), 1.01 (t, J = 7.3 Hz, 3 H), 0.92 (d, J = 7.0 Hz, 3 H), 0.82 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (δ) CO, 73.8, C, 146.4, 140.6, CH, 128.1, 126.9, 124.3, 59.3, 47.4, 46.3, 29.7, CH_2, 63.0, 34.5, 34.0, 25.0, 22.3, CH_3, 23.4, 20.9, 16.9, 12.2; IR (neat, cm^{-1}) 2960, 2930, 1464, 1452, 1384, 1368. Anal. Calcd for $C_{22}H_{32}O$: C, 84.62; H, 10.26. Found: C, 84.45; H, 10.18.

(1*S,2*R**,5*R**,6*R**)-8-Ethyl-2-methyl-5-(methylethyl)-bicyclo[4.3.0.]non-7-en-2-ol (2).** Alkene **9** (518 mg, 1.7 mmol) was dissolved in 5 mL of dry THF in a three-neck round-bottom flask fitted with a dry ice condenser and chilled to −78 °C. Twenty mL of ammonia was condensed into the reaction flask, and sodium metal (300 mg, 13.0 mmol) was added in small portions to give a deep blue solution. The reaction mixture was stirred for 30 min at −78 °C, and then NH_4Cl (695 mg, 13.0 mmol) was added and the reaction was warmed to rt while allowing a stream of N_2 to pass over it. Ethyl acetate and water were added, and the two layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 200 mL), and the combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was chromatographed to give **2** (255 mg, 70% yield) as a colorless oil which solidified on standing (mp = 50−52 °C): TLC R_f (10% ethyl acetate in hexanes) = 0.45; ^{1}H NMR (δ) 5.50 (bs, 1 H), 2.31 (bt, 1 H), 2.00−2.19 (m, 4 H), 1.93 (m, 1 H), 1.60−1.72 (m, 3 H), 1.23−1.42 (m, 4 H), 1.19 (s, 3 H), 1.12 (m, 1 H), 1.00 (t, J = 7.3 Hz, 3 H), 0.90 (d, J = 7.1 Hz, 3 H), 0.82 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (δ) CO, 70.2, C, 146.4, CH, 124.1, 57.8, 47.4, 47.2, 29.6, CH_2, 40.3, 33.9, 24.9, 22.3, CH_3, 28.5, 20.8, 16.9, 12.2; IR (neat, cm^{-1}) 3416, 2960, 2930, 1630 (weak), 1462, 1384, 1370; MS (m/z) 204 (30), 189 (16), 175 (19), 161 (100); HRMS calcd for $C_{15}H_{26}O$ 223.206 191, found 223.207 042.

(±)-Oxo-*T*-cadinol (1). Alcohol **2** (255 mg, 1.0 mmol) and 10 mg of Sudan III in 10 mL of methylene chloride were chilled to −78 °C. Ozone was passed through the reaction solution until the red Sudan III color faded. Nitrogen was then passed through the reaction for 10 min, and triphenylphosphine (399 mg, 1.5 mmol) was added. The mixture was allowed to warm to rt and stirred for 20 min, and then the solvent was removed *in vacuo*. The residue was dissolved in 20 mL of 5% (w/w) KOH in methanol and heated at reflux for 2 h. The reaction was then cooled and concentrated *in vacuo*. The residue was

chromatographed to give **1** (120 mg, 50% yield) as a viscous yellow oil: TLC R_f (30% ethyl acetate in hexanes) = 0.35; ^{1}H NMR (δ) 6.85 (bs, 1 H), 2.60 (m, 1 H), 2.39 (m, 2 H), 2.20 (m, 1 H), 1.79−1.65 (m, 5 H), 1.54−1.43 (m, 4 H), 1.17 (s, 3 H), 0.96 (d, J = 6.8 Hz, 3 H), 0.83 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (δ) C=O, 200.4, C, 135.0, CH, 147.0, 49.8, 45.1, 38.7, 26.4, CH_2, 39.9, 38.5, 19.4, CH_3, 28.1, 21.3, 15.9, 15.3; IR (neat, cm^{-1}) 3466, 2958, 1662, 1464, 1450, 1388, 1376; MS (m/z) 236 (21), 218 (36), 193 (13), 175 (100); HRMS calcd for $C_{15}H_{24}O_2$ 236.177630, found 236.177304. Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.27; H, 10.17; O, 13.56. Found: C, 76.15; H, 10.30; O, 13.62.

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Supporting Information Available: ^{1}H and ^{13}C spectra for all new compounds and input files for Discover generated by InsightII (33 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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