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Stereoselective Total Syntheses of (±)-Longicyclene, (±)-Longicamphor, and (±)-Longiborneol

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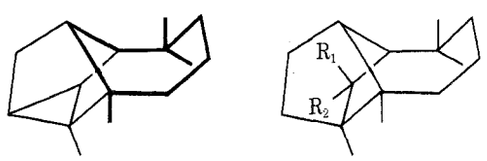
Stereoselective total syntheses of (±)-longicyclene (**1**), (±)-longicamphor **2A**), and (±)-longiborneol (**2B**) from tetrahydroeucarvone (**5**) *via* intermediate aldehyde **15** are reported. The synthetic approach contains a reductive cyclization reaction utilizing diisobutylaluminum hydride to construct bicyclic ketol **12.** A new sequence of reactions for converting cyclopropyl ketone **17** to (±)-longicyclene (**1**) without fragmentation is described.

The number of syntheses of sesquiterpene natural products has increased dramatically over the past 20 years, as indicated in recent reviews.[2] The sesquiterpene group of naturally occurring compounds contains a fantastic variety of intricately bridged molecular structures. This diversity of complex carbon skeletons provides the organic chemist with an excellent reservoir for exploring new synthetic methods and designs. The profusion of structural types requires a multitude of synthetic approaches challenging the imagination of many a synthetic organic chemist.

Synthetic quests within the longifolane class of sesquiterpenes have included such elaborately bridged structures as longifolene,[3,4] isolongifolene,[5] α-longipinene,[6,7] and culmorin.[8] The tetracyclic member of this interesting group of naturally occurring compounds, namely, longicyclene (**1**),[9] has evaded synthesis for nearly 10 years. A tricyclic member of the longifolane class, namely, longicamphor (**2A**), has previously been synthesized from (+)-longifolene *via* (+)-longiborneol (**2B**).[10] We wish to report herein stereoselective total syntheses of (±)-longicyclene (**1**), (±)-longicamphor (**2A**), and (±)-longiborneol (**2B**)[11] (Chart I).

Longicyclene (**1**), isolated from turpentine oil of *Pinus longifolia,* was assigned structure and absolute configuration **1** on the basis of spectral evidence and an acid-catalyzed conversion to longifolene.[9,12] Longicamphor (**2A**) is the corresponding oxidation product of longiborneol (**2B**). Longiborneol (juniperol, macrocarpol) was isolated from *Cupressus macrocarpa,* the famous Monterey cypress.[13,14]

Chart I
Longicyclene, Longicamphor, and Longiborneol



1 **2A**, $R_1, R_2 = O$; **B**, $R_1 = OH; R_2 = H$

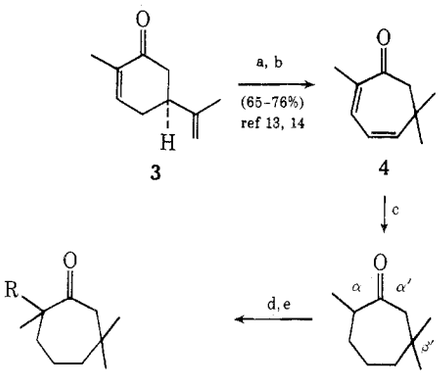
Results and Discussion

The starting material chosen for the synthesis of these sesquiterpenes is tetrahydroeucarvone (**5**). This ketone is readily available from (−)-carvone (**3**). Sequential treatment of carvone (**3**) with hydrogen bromide in glacial acetic acid followed by dehydrohalogenation using potassium hydroxide in methanol affords eucarvone (**4**) in 65–76% yield.[15,16] The mechanism of this rearrangement was studied by van Tamelen and coworkers. The reaction proceeds *via* a carenone intermediate which, in the presence of excess base, opens to give eucarvone (**4**).[17] Catalytic hydrogenation of dienone **4** neat over 10% palladium on carbon produces the desired starting ketone **5** in 94% yield.[18,19]

The basic carbon skeleton of ketone **5** can be seen in longicyclene (**1**) as outlined with heavy lines. The synthetic strategy was to prepare a bicyclo[4.2.1]nonane intermediate by constructing an appropriately functionalized two-carbon bridge between carbon-2 and carbon-7 of ketone **5.** With this goal in mind, the plan was to sequentially alkylate tetrahydroeucarvone selectively at the α-methine position and then to construct the two-carbon bridge by an intramolecular carbon–carbon bond-forming process at the α′-methylene position. In recent reviews both Conia[20] and House[21] point out that alkylation of an unsymmetrical cyclic ketone such as tetrahydroeucarvone (**5**), where the corresponding enolate is generated under thermodynamically controlled conditions, is favored at the α-methine position. The presence of an alkyl group, such as a methyl group, at an α position favors α-alkylation. The presence of alkyl substituents at the β′ position also favors α-alkylation. Whenever the two effects are combined, as in tetrahydroeucarvone (**5**), then α-alkylation should predominate.

Alkylation of Tetrahydroeucarvone (Chart II). Alkylation of tetrahydroeucarvone (**5**) by generating the enolate anion using stirred sodium hydride in 1,2-dimethoxyethane (DME) at 80 ± 5° for 24–48 hr followed by addition of allyl bromide gives keto olefin **6A** in 80% yield. Alkylation of the sodium enolate of ketone **5** with ethyl 2-bromoacetate affords keto ester **6B** in 53% yield. The structures of both alkylation products **6A** and **6B** were confirmed by spectroscopic data. Both compound **6A** and **6B** show an AB quartet in the nmr spectrum for two methylene protons adjacent to a ketone carbonyl (–$COCH_2$ centered at δ 2.38,

Chart II
Alkylation of Tetrahydroeucarvone[a]



3 4 5 6

6 R
A $-CH_2CH{=}CH_2$ (80%)
B $-CH_2CO_2Et$ (53%)
C $-CH(CH_3)CH{=}CHCH_3$ (86%)
D $-CH(CH_3)CO_2Et$ (33%)

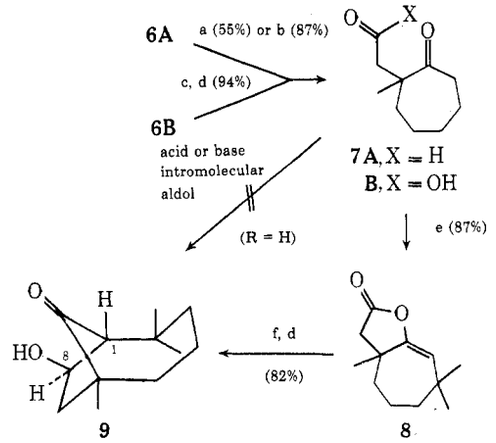
[a] a, HBr, HOAc; b, KOH, CH_3OH; c, H_2, 10% Pd/C; d, NaH, DME, Δ 24–48 hr; e, $BrCH_2CH{=}CH_2$, $BrCH_2CO_2Et$, $CH_3CHClCH{=}CHCH_3$, or $CH_3CHBrCO_2Et$ for products **6A, 6B, 6C,** and **6D,** respectively.

J_{AB} = 11 Hz, and δ 2.37, J_{AB} = 14 Hz, for compounds **6A** and **6B,** respectively). No isomeric alkylated products at the methylene position were observed spectroscopically (nmr) or detected chromatographically (glc). The sodium enolate of tetrahydroeucarvone was also alkylated, similarly, with 4-chloro-2-pentene[22,23] to produce keto olefin **6C** in 86% yield, and with ethyl 2-bromopropanoate to give keto ester **6D** in 33% yield.[8,24]

Model Study to Prepare an Appropriately Functionalized Bicyclo[4.2.1]nonane Intermediate (Chart III). Oxidative cleavage of keto olefin **6A** using osmium tetroxide and 2.1 equiv of sodium metaperiodate in aqueous tetrahydrofuran (THF) produced keto aldehyde **7A** in 55% yield.[25] All attempts to affect an intramolecular aldol cyclization to ketol **9** using either acid or base catalysis gave only recovered starting keto aldehyde **7A.**[26]

Oxidative cleavage of keto olefin **6A** using a catalytic amount of ruthenium tetroxide and 5.4 equiv of sodium metaperiodate in aqueous *tert*-butyl alcohol gave keto acid **7B** in 87% yield.[27] Keto acid **7B** was also prepared from keto ester **6B** in 94% yield by saponification with potassium hydroxide in aqueous methanol followed by acidification with dilute hydrochloric acid. Keto acid **7B** was converted to enol lactone **8** in 87% yield by treatment with anhydrous sodium acetate in refluxing acetic anhydride for 5 hr.[28] Reduction of enol lactone **8** with 1.1 equiv of diisobutylaluminum hydride in anhydrous tetrahydrofuran (THF) at room temperature for 22 hr followed by neutralization with dilute hydrochloric acid at 0° (ice bath) gave crystalline bicyclic ketol **9** in 82% yield. Other reducing agents such as lithium tri-*tert*-butoxyaluminum hydride or lithium trimethoxyaluminum hydride proved unsuccessful.[28] The β configuration for the alcohol group was assigned on the basis of nmr data. A vicinal coupling constant of $J_{1,8}$ = 2 Hz was observed for the bridgehead proton at carbon-1 coupled with the hydroxymethine proton at carbon-8. The magnitude of this coupling constant is in accord with a dihedral angle near 130°.[29,30] Examination of a Dreiding model of exo alcohol **9** shows an expected dihedral angle near 130° in keeping with the observed coupling constant. The endo isomer of structure **9** would have an expected dihedral angle near 15° (from Dreiding models) which should exhibit a vicinal coupling constant near J = 7.7 Hz for the bridgehead proton on carbon-1.

Chart III
Model Study[a]

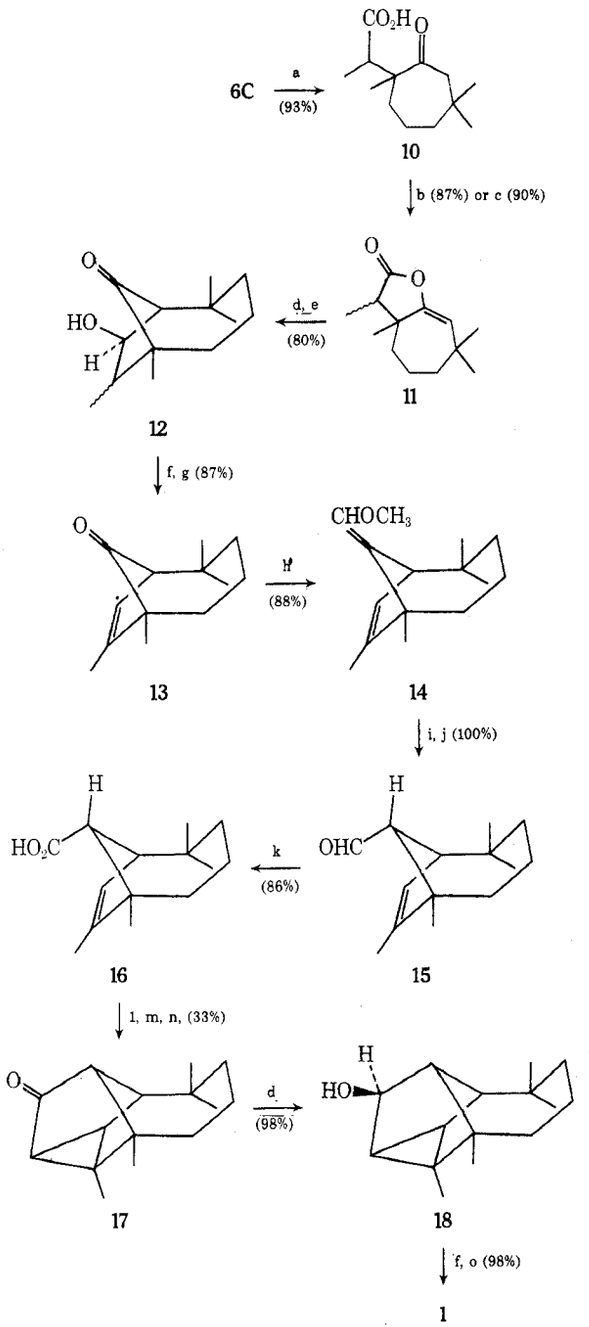


9 8

[a] a, OsO_4, $NaIO_4$, H_2O, THF, for **7A;** b, RuO_4, $NaIO_4$, H_2O, *t*-BuOH, for **7B;** c, KOH, CH_3OH, H_2O; d, H_3O^+; e, NaOAc, Ac_2O, Δ; f, *i*-Bu_2AlH, THF.

Synthesis of (±)-Longicyclene (1) (Chart IV). Oxidative cleavage of keto olefin **6C** using catalytic amounts of ruthenium tetroxide–osmium tetroxide and 5 equiv of sodium metaperiodate in aqueous *tert*-butyl alcohol gave keto acid **10** in 93% yield.[27] The use of catalytic amounts of only ruthenium tetroxide resulted in much lower yields. Keto acid **10** was converted to enol lactone **11** by two methods. First, treatment of compound **10** with anhydrous sodium acetate in refluxing acetic anhydride for 5 hr gave enol lactone **11** in 87% yield.[28] Second, a solution of keto acid **10,** acetic anhydride, and a catalytic amount of 60% perchloric acid in dichloromethane was allowed to stir at room temperature for 4 hr to afford enol lactone **11** in 90% yield.[31] Reductive cyclization of enol lactone **11** using 1.1 equiv of diisobutylaluminum hydride in anhydrous tetrahydrofuran (THF) at 60° (bath temperature) for 18 hr followed by neutralizing the reaction mixture with dilute hydrochloric acid at 0° (ice bath) produced liquid bicyclic ketol **12** as a 66:34 mixture of diastereomers (glc) in 80% yield.[28] This bicyclic ketol was found to be extremely sensitive to either base- or acid-catalyzed fragmentation to a keto aldehyde. Bicyclic ketol **12** was immediately esterified with methanesulfonyl chloride in dichloromethane in the presence of triethylamine.[32] The crude mesylate ester was stirred in collidine at 170–175° for 16 hr to afford bicyclic enone **13** in 87% overall yield from ketol **12.**[33] The infrared data for bicyclic enone **13** were in good agreement with that reported for the same structure as a degradation product of culmorin by Barton and Werstiuk.[34] A Wittig reaction on enone **13** using methoxymethylenetriphenylphosphorane in dimethyl sulfoxide at 60° gave methoxyvinyl ether **14** in 88% yield.[35] Hydrolysis of methoxyvinyl ether **14** in a homogeneous solution of 50% perchloric acid in ether for 1.75 hr followed by epimerization of the resulting mixture of aldehydes with anhydrous potassium carbonate in methanol at room temperature for 1.75 hr produced aldehyde **15** in quantitative yield.[35] Aldehyde **15** was smoothly oxidized to carboxylic acid **16** utilizing Jones reagent in acetone at room temperature for 30 min.[36,37] Acid **16** was converted to an acid chloride using oxalyl chloride in benzene. The crude acid chloride was then treated with anhydrous diazomethane in ether to afford an intermediate diazo ketone. This diazo ketone was stirred with a suspension of copper powder in refluxing tetrahydrofuran to produce crystalline

Chart IV
Synthesis of (±)-Longicyclene[a]

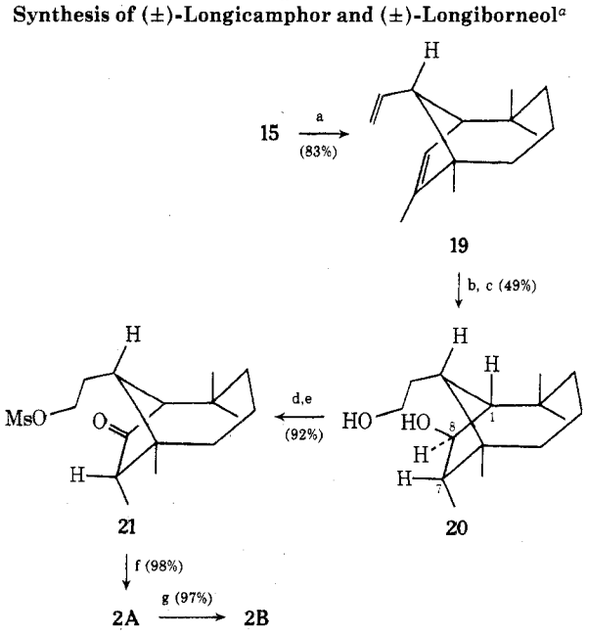


[a] a, RuO_4, OsO_4, H_2O, *t*-BuOH, $NaIO_4$; b, NaOAc, Ac_2O, Δ; c, Ac_2O, CH_2Cl_2, $HClO_4$ (catalytic); d, *i*-Bu_2AlH, THF; e, H_3O^+; f, MsCl, CH_2Cl_2, Et_3N; g, collidine, Δ; h, $Ph_3P{=}CHOCH_3$, DMSO, Δ; i, $HClO_4$, H_2O, Et_2O; j, K_2CO_3, CH_3OH; k, CrO_3, H_2SO_4, acetone; l, $(COCl)_2$, PhH; m, CH_2N_2, Et_2O; n, Cu, THF, Δ; o, $LiAlH_4$, Et_2O.

tetracyclic cyclopropyl ketone **17** in 33% overall yield from carboxylic acid **16**.[38] Two modificiations of the Wolff–Kishner reduction of cyclopropyl ketone **17** were attempted and both (Huang-Minlon procedure and Nagata–Itazaki modification) were unsuccessful.[39-41] Both attempts afforded mostly starting material plus minor amounts of unidentified cleavage products. Even an attempt to prepare the tosylhydrazone derivative of ketone **17** under forcing conditions gave only recovered starting material. Examination of a Drieding model of cyclopropyl ketone **17** shows that the β side of the carbonyl carbon atom is hindered by the methyl substituents at carbon-1 and carbon-11, but relatively unhindered on the α side of the carbonyl. Reduction of ketone **17** with diisobutylaluminum hydride in tetrahydrofuran produced crystalline cyclopropylcarbinyl alcohol **18** in 98% yield. The stereochemistry of alcohol **18** was assigned on the basis of "steric approach control."[42] The bulky hydride reagent should approach from the less hindered face of the carbonyl to afford an alcohol with the stereochemistry indicated by structure **18**. Alcohol **18** was esterified with methanesulfonyl chloride in dichloromethane in the presence of triethylamine at −15° (freezer) for 72 hr.[32] The entire reaction mixture was then added to a mixture of lithium aluminum hydride in ether. This mixture was stirred at reflux to afford (±)-longicyclene (**1**) in 98% overall yield from alcohol **18**. No fragmentation of the cyclopropane ring to give olefinic products was observed (nmr, glc). The synthetic (±)-longicyclene was identical with an authentic sample of (+)-longicylene[9] with respect to ir, nmr, and glc retention times on five columns.

Synthesis of (±)-Longicamphor (2A) and Longiborneol (2B) (Chart V). The synthesis of (±)-longicamphor (**2A**) and (±)-longiborneol (**2B**) utilizes bicyclic aldehyde **15** as the key synthetic intermediate. A Wittig reaction on aldehyde **15** using methylenetriphenylphosphorane in dimethyl sulfoxide at room temperature for 13.5 hr gave diene **19** in 83% yield.[35] Hydroboration of diene **19** with diborane in anhydrous tetrahydrofuran followed by oxidation using basic hydrogen peroxide produced crystalline diol **20** in 49% yield.[43] An attempt to increase the yield for this conversion utilizing disiamylborane in tetrahydrofuran followed by basic hydrogen peroxide gave nearly identical results.[43] First-order analysis of the coupling constants for the hydroxymethine proton at carbon-8 (the X part of an AMX system) shows coupling constants of J = 2.6 and 7.8 Hz. Routine use of europium(DPM)$_3$[44] sufficiently dispersed the nmr spectrum so that the bridgehead proton on carbon-1 was clearly observable, thus establishing the coupling constant $J_{1,8}$ = 2.6 Hz. The magnitude of this coupling constant is in agreement with a dihedral angle near 120° for the vicinal protons on carbon-1 and carbon-8. This dihedral angle is what would be expected for exo alcohol **20**

Chart V
Synthesis of (±)-Longicamphor and (±)-Longiborneol[a]



[a] a, $Ph_3P{=}CH_2$, DMSO, room temperature; b, BH_3·THF; c, H_2O_2, OH^-; d, MsCl, CH_2Cl_2, Et_3N; e, CrO_3·py_2, CH_2Cl_2; f, $NaN(SiMe_3)_2$, PhH, DME; g, Ca, NH_3, *n*-PrOH.

based on examination of the Dreiding model for structure **20**.[29,30] Examination of the Dreiding model for the endo isomer of structure **20** shows an expected dihedral angle near 0° and the predicted coupling constant would have to be near 8 Hz.[29,30] The tricyclic carbon framework of longicamphor (**2A**) was constructed from diol **20** using an intramolecular alkylation sequence similar to that employed by Johnson and coworkers in their synthesis of aldosterone.[45] The primary alcohol was selectively esterified using 1.1 equiv of methanesulfonyl chloride in dichloromethane in the presence of triethylamine.[32] The crude liquid hydroxymesylate ester was oxidized using chromium trioxide–dipyridine complex in dry dichloromethane[46,47] to afford crystalline keto mesylate **21** in 92% overall yield from diol **20**. Treatment of keto mesylate **21** with sodium bis(trimethylsilyl)amide[48] in benzene–1,2-dimethoxyethane at room temperature for 40 min gave (±)-longicamphor (**2A**) in 98% yield.[49] The synthetic (±)-longicamphor was identical with natural (+)-longicamphor with respect to ir, nmr, and glc retention times on five columns. Reduction of (±)-longicamphor (**2A**) with calcium metal in liquid ammonia in the presence of 1-propanol produced (±)-longiborneol (**2B**) in 97% yield.[10,12,13,34,49] The synthetic (±)-longiborneol was identical with natural (+)-longiborneol (prepared from (+)-longicamphor) with respect to ir, nmr, and glc retention times on five columns.

Experimental Section

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. All boiling points are uncorrected. Analyses were performed by Elek Microanalytical Laboratories, Torrance, Calif., and Spang Microanalytical Laboratory, Ann Arbor, Mich.

Analytical gas phase chromatography (glc) was performed using the following types of columns of flow rates: (A) 50-ft, stainless steel, 0.02-in. capillary column coated with Carbowax 6000, flow rate 5 ml/min at ambient temperature; (B) 300-ft, stainless steel, 0.02-in. capillary column coated with OV-17 (Varian), flow rate 5 ml/min at ambient temperature; (C) 300-ft, stainless steel, 0.02-in. capillary column coated with FFAP (Varian), flow rate 5 ml/min, at ambient temperature; (D) 5-ft, stainless steel, 0.125-in. column, packed with 3% SE-30 on Varaport 30, 100/120 mesh (Varian), flow rate 15 ml/min at ambient temperature; (E) 6-ft, stainless steel, 0.125-in. column, packed with 5% FFAP on Varaport-30, 80/100 mesh (Varian), flow rate 15 ml/min at ambient temperature; (F) 6-ft, stainless steel, 0.125-in. column, packed with 5% OV-17 on Varaport-30, 80/100 mesh (Varian), flow rate 15 ml/min at ambient temperature.

Silica gel $PF_{254+366}$ (E. Merck No. 7748) and silica gel 60 (E. Merck No. 7734, 70–230 or 75–325 mesh) available from Brinkmann Instruments were used for thin layer and column chromatography, respectively.

Infrared (ir) spectra were recorded on a Perkin-Elmer Model 337 or 700 spectrophotometer. Solid samples were recorded in spectroquality carbon tetrachloride or chloroform using 0.10-mm sodium chloride cells. Liquid samples were taken as thin films between sodium chloride plates.

Nuclear magnetic resonance (nmr) spectra were measured on a Varian Associates Model T-60 or HA-100 spectrometer. The following abbreviations are used to describe nmr spectral bands reported in the Experimental Section: broad (b), singlet (s), doublet (d), triplet (t), quartet (q), AB quartet (AB), multiplet (m), and δ (parts per million, ppm) downfield from tetramethylsilane.

Finally, for all reactions performed under an atmosphere of dry nitrogen, the equipment was dried in an oven at 120° for several hours, then allowed to cool in an atmosphere of dry nitrogen using an apparatus designed by Johnson and Schneider.[50] All liquid transfers were made with nitrogen-filled syringes. Petroleum ether refers to Baker Analyzed reagent, bp 30–60°.

Eucarvone (4).[15,16] Freshly distilled carvone (**3**, 200 g, 1.33 mol) was slowly added to a solution of anhydrous hydrogen bromide (295 g, 3.66 mol) in glacial acetic acid (1.0 l.) at 5–10° with rapid stirring and efficient cooling. The cooling bath was removed and stirring was continued for 15 min.

The resulting orange solution was poured into water (2 l.), the lower layer was separated, and the aqueous layer was extracted with ether (three times). The combined ethereal extracts were washed with water (three times), saturated potassium bicarbonate solution until basic to litmus paper, and finally water until neutral. The organic solution was dried (Na_2SO_4) and then added dropwise to a well-stirred and cooled solution of potassium hydroxide (145 g) and anhydrous methanol (550 ml).

After completion of the addition, the resulting suspension was stirred at reflux for 15 min and then poured into ice–sulfuric acid. The yellow liquid was separated and the aqueous layer was extracted with ether (three times). The combined ethereal extracts were washed with 10% sodium hydroxide (three times) to remove the carvacrol and then with water until neutral, dried (Na_2SO_4), concentrated *in vacuo*, and distilled to give 130 g (65%) of eucarvone (**4**): bp 46–49° (1.5 mm) [lit.[16] bp 81.5–84.0° (8 mm)]; ir (film) 3010 (CH=CH), 1660 (CO), 1385, 1365 (*gem*-CH_3), and 728 cm^{-1} (CH=CH); nmr (CCl_4) δ 5.5–6.54 (m, 3, CH=CH), 2.57 (s, 2, $COCH_2$), 1.85 (d, 3, J = 1.8 Hz, CH_3C=), and 1.06 ppm (s, 6, *gem*-CH_3).

Tetrahydroeucarvone (5).[18,19] Eucarvone (**4**, 223 g, 1.49 mol) was carefully mixed with 10% palladium on charcoal (8.5 g) in a Parr Shaker bottle. The unsaturated ketone was hydrogenated on a Parr Shaker at 15–50 psi until no further hydrogen uptake was observed. The product was filtered through Celite and distilled to give 215 g (94%) of tetrahydroeucarvone (**5**): bp 47–50° (1.5 mm) [lit.[18,19] bp 46–49° (1.5 mm)]; ir (film) 1700 (CO), 1385, and 1370 cm^{-1} (*gem*-CH_3); nmr (CCl_4) δ 2.34 (distorted AB, 3, J_{AB} = 12 Hz, CHCO and $COCH_2$), 1.02 (d, 3, J = Hz, CH_3CH), 0.95 and 0.91 ppm (s, s, 6, *gem*-CH_3); nmr (100 Hz, CCl_4) δ 2.21 (distorted AB, 3, J_{AB} = 12 Hz, CHCO and $COCH_2$), 0.88 (d, 3, J = 7 Hz, CH_3CH), 0.83 and 0.78 ppm (s, s, 6, *gem*-CH_3).

2-(3′-Propene)-2,6,6-trimethylcycloheptanone (6A). Sodium hydride (1.63 g, 40 mg-atoms of a 59% dispersion) was transferred to the reaction flask and washed with anhydrous 1,2-dimethoxyethane (DME, 5 × 10 ml freshly distilled from lithium aluminum hydride). Dry DME (10 ml) was added and the apparatus was sealed under dry nitrogen. Tetrahydroeucarvone (**5**, 6.00 g, 38.9 mmol) dissolved in dry DME (10 ml) was added. The mixture was allowed to stir at 80 ± 2° for 48 hr.

The resulting light yellow slurry of sodium enolate was cooled to room temperature and allyl bromide (7.0 ml, 80 mmol, freshly distilled) dissolved in dry DME (5 ml) was added over a period of 1 hr. The pale yellow slurry was allowed to stir at room temperature for 24 hr and then poured into a mixture of acetic acid, ice, and ether. The ether layer was separated, washed with 10% sodium bicarbonate solution (three times) and water (three times), and then dried (Na_2SO_4) and concentrated *in vacuo*. Distillation gave 6.05 g (80%) of colorless alkylated ketone **6A:** bp 49.5–50.5° (0.17 mm); ir (film) 3075 ($CH=CH_2$), 1695 (CO), 1640 ($CH=CH_2$), 1460 (CH), 1390, 1370, 1365 (*gem*-CH_3), 993 and 912 cm^{-1} ($CH=CH_2$); nmr (CCl_4) δ 4.8–6.1 (m, 3, $CH=CH_2$), 2.38 (AB, 2, J_{AB} = 11 Hz, $COCH_2$), 2.14 (d, 2, J = 8 Hz, $CH_2CH=CH_2$) 0.99, 0.95 and 0.89 ppm (s, s, s, 9, CH_3); glc analysis on column A (column temperature 120°, retention time 12.1 min) shows the product to be greater than 99.6% of a single product.

Anal. Calcd for $C_{13}H_{22}O$: C, 80.36; H, 11.41. Found: C, 80.39; H, 11.46.

2-(Ethyl 2′-acetate)-2,6,6-trimethylcycloheptanone (6B).[24] Sodium hydride (1.79 g, 44 mg-atoms of a 59% dispersion) was transferred to the reaction flask and washed with anhydrous 1,2-dimethoxyethane (DME, 3 × 10 ml, freshly distilled from lithium aluminum hydride). Dry DME (35 ml) was added and the flask was sealed under dry nitrogen. Tetrahydroeucarvone (**5**, 6.00 g, 38.9 mmol, dissolved in dry DME, 5 ml) was added to the stirred sodium hydride in refluxing DME. The mixture was allowed to stir at 82 ± 3° for 46 hr.

The resulting light yellow slurry of enolate anion was cooled to 15° and ethyl 2-bromoacetate (4.9 ml, 44 mmol, freshly distilled) dissolved in dry DME (5 ml) was added over a period of 5 min. The reaction mixture was allowed to warm to 25° over a period of 90 min and then poured into acetic acid–ice and extracted with ether. The combined ethereal extracts were washed with saturated sodium bicarbonate solution (three times) and with saturated sodium chloride solution until neutral, and then dried ($MgSO_4$) and concentrated *in vacuo*. Distillation gave 4.80 g (53%) of colorless keto ester **6B:** bp 76.5–79° (0.08 mm); ir (film) 1735 (CO_2Et), 1700 (CO), 1395, 1380, 1365 (*gem*-CH_3), 1228, 1200, 1161 (asymmetric COC), 1118, 1066, and 1033 cm^{-1} (symmetric COC); nmr (CCl_4) δ 4.06 (q, J = 7 Hz, OCH_2CH_3), 2.43 (bs, 2, CH_2CO_2Et), 1.10 (s, 3,

CH_3), and 0.91 ppm (s, 6, *gem*-CH_3O); glc analysis on column A (column temperature 120° retention time 20.5 min) shows the keto ester to be greater than 99.6% of a single product.

Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.06. Found: C, 70.25; H, 10.03.

3-Penten-2-ol.[22,23] **Method A.** An ethereal solution of methyllithium (Alfa Inorganics, 1.6 *M* solution, 550 ml) was transferred to the reaction flask under nitrogen. Freshly distilled crotonaldehyde (60.0 g, 856 mmol) was placed in a dropping funnel. The apparatus was sealed under dry nitrogen. The crotonaldehyde was added dropwise to the rapidly stirred methyllithium solution at 0° (ice bath) over a period of 2 hr.

The resulting light yellow reaction mixture was allowed to stir for 30 min and then carefully quenched with distilled water (100 ml). The inorganic salts were removed by filtration and the ether layer was separated. The ethereal solution was washed with saturated sodium chloride solution (three times), dried (Na_2SO_4), and concentrated *in vacuo* at room temperature. A trace of anhydrous calcium oxide was added and the crude product was distilled to give 35 g (47%) of 3-penten-2-ol, bp 119–122° (lit.[22,23] bp 119–122°).

Method B. Approximately 3.0 l. of anhydrous ether and 122 g (5.0 g-atoms) of magnesium turnings were placed in a 5-l. three-necked flask. Methyl iodide (324 ml, 5.2 mmol) was placed in a pressure-compensating dropping funnel.

After the first 50 ml of methyl iodide had been added, the flask was gently warmed to initiate the reaction. The remainder of the methyl iodide was added at a rate which would maintain the reaction at gentle reflux.

When most of the magnesium had reacted, crotonaldehyde (284 g, 4.04 mol, dissolved in anhydrous ether, 300 ml) was added dropwise with vigorous stirring and cooling (ice bath). The mixture was then allowed to stir at room temperature for 30 min, quenched with saturated sodium chloride solution (500 ml) with cooling (ice bath), the ether layer decanted, washed with 10% sodium sulfite solution (three times), dried (K_2CO_3–Na_2SO_4), filtered, and concentrated *in vacuo* at room temperature. A trace of anhydrous calcium oxide was added and the crude product was distilled to give 286 g (82%) of colorless 3-penten-2-ol: bp 119–122°; ir (film) 3650–3050 (OH), 3025 (CH=CH), 1675 (trans CH=CH), 1450, 1375, 1360 (CH_3), 1060, 1021 (OH), 962 (trans CH=CH), 909, and 858 cm^{-1}; nmr (CCl_4) δ 5.17–5.97 (m, 2, CH=CH), 4.36 (bm, 1, CHOH), 4.13 (bm, 1, CHOH), 1.67 (doublet of doublets, 3, J_1 = 1, J_2 = 4.2 Hz, CH_3CH=CH), and 1.14 ppm (d, 3, J_3 = CH_3CH).

4-Chloro-2-pentene.[22] **Method A.** Zinc chloride (53.6 g, 395 mmol, previously dried at 110° for 24 hr) was dissolved in concentrated hydrochloric acid (100 ml) and cooled at 0° (ice bath). 3-Penten-2-ol (34.0 g, 395 mmol) was added all at once and the solution was stirred at 1–10° for 90 min. The mixture was transferred to a separatory funnel. The organic layer was separated, washed with saturated sodium chloride solution (three times), dried ($CaCl_2$), and distilled to give 28.1 g (68%) of 4-chloro-2-pentene, bp 99–102° (lit.[22] bp 100.5°).

Method B. 3-Penten-2-ol (73.1 g, 849 mmol) was placed in a 100-ml round-bottomed flask and cooled to 0° (ice bath). Anhydrous hydrogen chloride gas was slowly bubbled through the alcohol for 3 hr. The mixture was then transferred to a separatory funnel and the aqueous layer was separated. The crude chloride was dried ($CaCl_2$) and distilled to give 68.8 g (77%) of 4-chloro-2-pentene: bp 99–102°; ir (film) 3040 (w, CH=CH), 1670 (trans CH=CH), 1450, 1375 (CH_3), 961 (trans CH=CH), and 643 cm^{-1} (CHCl); nmr (CCl_4) δ 5.28–6.06 (m, 2, CH=CH), 4.22–5.0 (m, 1, CHCl), 1.63 (doublet of doublets, 3, J_1 = 1, J_2 = 5 Hz, CH_3CH=CH), and 1.49 ppm (d, 3, J_3 = 6.3 Hz, CH_3CHCl).

2-(4′-Pent-2′-ene)-2,6,6-trimethylcycloheptanone (6C).[8,24] Sodium hydride (17.9 g, 440 mg-atoms of a 59% dispersion) was transferred to the flask and washed with anhydrous 1,2-dimethoxyethane (DME, 3 × 25 ml, freshly distilled from lithium aluminum hydride). Dry DME (250 ml) was added and the apparatus was sealed under dry nitrogen. Tetrahydroeucarvone (**5**, 60.0 g, 389 mmol, dissolved in dry DME, 50 ml) was added rapidly. The reaction mixture was allowed to stir at 80 ± 5° for 72 hr.

To the resulting light yellow slurry of sodium enolate at 5° (ice bath) was added 4-chloro-2-pentene (46.5 g, 440 mmol, dissolved in dry DME, 50 ml). The reaction mixture was allowed to stir at room temperature for 72 hr.

The resulting milky-white slurry was heated to reflux (2 hr), cooled, poured into ice–water, and extracted with ether. The combined ethereal extracts were washed with saturated sodium chloride solution until neutral, dried ($MgSO_4$), and concentrated *in vacuo*. Distillation gave 74 g (86%) of colorless alkylated ketone **6C:** bp 70–71° (0.16 mm); ir (film) 3025 (CH=CH), 1695 (CO), 1675 (trans CH=CH), 1390, 1380, 1370 (*gem*-CH_3) and 966 cm^{-1} (trans CH=CH); nmr (CCl_4) δ 4.67–5.16 (m, 2, CH=CH), 2.63, 2.47 (two doublets, 1, J = 2.2, J_2 = 1.7, J_4 = 1.7 Hz, CH_3CHCH=CH), 0.92, 0.85, 0.77 (s, s, s, 9, CH_3), and 0.74 ppm (d, 3, J_5 = 6.6 Hz, CH_3CH).

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.14; H, 11.73.

2-(Ethyl 2′-propanoate)-2,6,6-trimethylcycloheptanone (6D).[8,24] Sodium hydride (17.9 g, 440 mg-atoms of a 59% dispersion) was transferred to the reaction flask and washed with anhydrous 1,2-dimethoxyethane (DME, 3 × 25 ml, freshly distilled from lithium aluminum hydride). Dry DME (500 ml) was then distilled directly into the flask. The apparatus was sealed under dry nitrogen. The slurry was stirred at 82 ± 2° while tetrahydroeucarvone (**5**, 60.0 g, 389 mmol, dissolved in dry DME, 100 ml) was added. The mixture was allowed to stir at 82 ± 2° for 73 hr.

The resulting light yellow slurry of sodium enolate was cooled to 0° (ice bath) and ethyl 2-bromopropanoate (57.4 ml, 441 mmol, freshly distilled) dissolved in dry DME (100 ml) was added very rapidly. The reaction mixture was allowed to warm to room temperature over a period of 1 hr, poured into acetic acid–ice, and extracted with ether. The combined ethereal extracts were washed with saturated sodium bicarbonate solution (three times) and saturated sodium chloride solution until neutral, and then dried ($MgSO_4$) and concentrated *in vacuo*. Distillation gave 32 g (33%) of colorless keto ester **6D:** bp 84–104° (0.06 mm); ir (film) 1735 (CO_2Et), 1700 (CO), 1385, 1365 (*gem*-CH_3) 1280, 1260, 1250, 1220 (asymmetric COC), 1190–1160 cm^{-1} (symmetric COC); nmr (CCl_4) δ 4.12 (q, J = 7.2 Hz, OCH_2CH_3), 4.04 (q, J = 7.2 Hz, OCH_2CH_3), two diastereomers), 1.24 (d, J = 3.2 Hz, CH_3CH), 1.04 (t, J = 7.2 Hz, OCH_2CH_3), and 0.85 ppm (s, CH_3).

Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 71.00; H, 10.05.

2-(2′-Ethanal)-2,6,6-trimethylcycloheptanone (7A).[25] Osmium tetroxide solution was prepared by dissolving 1.00 g (3.94 mmol) of osmium tetroxide in distilled water (100 ml).

Unsaturated ketone **6A** (5.00 g, 25.8 mmol) and an aqueous solution of tetrahydrofuran [100 ml of a 1:3 solution (v/v) of water–THF] were transferred to the reaction flask. Sodium metaperiodate (11.6 g, 54.5 mg-atoms, Matheson) was placed in the solid addition funnel. The solution was stirred under a constant flow of nitrogen while osmium tetroxide solution (5.0 ml, 1.97 × 10^{-1} mmol) was added. Immediately a light brown color appeared. The sodium metaperiodate was added in small portions over a period of 1 hr. The reaction flask was sealed under dry nitrogen and allowed to stir at room temperature for 3 hr. The resulting white slurry was filtered and the filtrate was extracted with ether. The combined ethereal extracts were washed with water (three times), dried ($MgSO_4$), and concentrated *in vacuo*. Distillation gave 2.80 g (55%) of colorless keto aldehyde **7A:** bp 78–79° (0.20 mm); ir (film) 2735, 1720 (CHO), 1695 (CO), 1390, 1375, 1365 cm^{-1} (*gem*-CH_3); nmr (CCl_4) δ 9.75 (t, 1, J = 2.3 Hz, CHO), 2.46 (AB, 2, J_{AB} = 11 Hz, $COCH_2$), 2.45, 2.32 (pair of d, 2, J = 2.3 Hz, CH_2CHO), 1.22, 0.96, and 0.90 ppm (s, s, s, 9, CH_3).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.15; H, 10.11.

2-(2′-Ethanoic acid)-2,6,6-trimethylcycloheptanone (7B). Method A.[27] A solution of sodium metaperiodate (45 g, 210 mg-atoms), keto olefin **6A** (6.94 g, 38.9 mmol), aqueous ruthenium trichloride solution (0.6 ml, 0.038 g/ml, 0.0231 g) in distilled water (1600 ml), and *tert*-butyl alcohol (500 ml) was stirred at room temperature for 72 hr. The solution was transferred to a separatory funnel and extracted with dichloromethane (6 × 150 ml). The combined organic extracts were washed with 10% sodium hydroxide solution (5 × 100 ml). The combined basic extracts were washed with dichloromethane (50 ml). The aqueous layer was acidified with concentrated hydrochloric acid and extracted with dichloromethane (5 × 100 ml). The combined latter organic extracts were washed with saturated sodium chloride solution, dried ($MgSO_4$), and concentrated *in vacuo* to 7.52 g of a yellow, viscous oil. Distillation gave 7.16 g (87%) of f a slightly yellow, viscous keto acid **7B.**

Method B. A solution of keto ester **6B** (12.36 g, 5.13 mmol) and potassium hydroxide (10.0 g) in methanol (150 ml) and water (50 ml) was stirred at room temperature for 13 hr and then allowed to reflux for 1 hr.

The light yellow solution was cooled to room temperature and extracted with ether in order to remove neutral side products. The

aqueous layer was acidified with concentrated hydrochloric acid and again extracted with ether. The combined latter ethereal extracts were washed with saturated sodium chloride solution, dried ($MgSO_4$), and concentrated *in vacuo* to give 10.2 g (94%) of slightly yellow, viscous keto acid **7B:** bp 100° (bath temperature, 0.30 mm); ir (film) 2450–3650 (CO_2H), 1735, 1700 (CO_2H), 1380, 1360 (*gem*-CH_3), 1291, 1224, 1200 cm^{-1} (CO); nmr (CCl_4) δ 10.0 (s, 1, CO_2H), 2.40 (m, 0.4, CH_2CO), 1.19, 0.95, 0.92 ppm (s, s, s, 9, CH_3).

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.65; H, 9.41.

3,3,7-Trimethyl-9-oxo-10-oxabicyclo[5.3.0]dec-1-ene (8).[28] A solution of keto acid **7B** (9.10 g, 42.9 mmol) and anhydrous sodium acetate (0.5 g) in acetic anhydride was allowed to stir at 140 ± 2° (bath temperature) for 5 hr.

The resulting orange-brown solution was cooled to room temperature, poured into ice-saturated sodium bicarbonate solution (300 g–150 ml), and extracted with ether (5 × 50 ml). The combined ethereal extracts were washed with water (3 × 50 ml) and saturated sodium chloride solution (50 ml), dried (Na_2SO_4), and concentrated *in vacuo*. The remaining traces of acetic anhydride were removed by codistillation *in vacuo* with toluene (3 × 50 ml) and with methanol (3 × 50 ml, containing a trace of pyridine). The orange oil was dissolved in hexane (50 ml), concentrated to approximately 25 ml, and cooled in the freezer overnight. The crude, slightly yellow crystals were purified by sublimation (40 ± 2°, 0.5 mm) to give 7.26 g (87%) of pure white, crystalline enol lactone **8:** mp 68.7–69.2°; ir ($CHCl_3$) 1800, 1790 (CO), 1685 (OC=CH), 1390, 1380, 1365 (*gem*-CH_3), 857 and 848 cm^{-1} (C=CH); nmr (CCl_4) δ 5.06 (s, 1, OC=CH), 2.36 (AB, 2, J_{AB} = 17 Hz, CH_2CO), 1.28 (s, 3, CH_3), and 1.05 ppm (bs, 6, *gem*-CH_3).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.38; H, 9.35.

2,2,6-Trimethyl-8-*exo*-hydroxybicyclo[4.2.1]nonan-9-one (9).[28] Enol lactone **8** (0.120 g, 0.619 mmol) was stirred in anhydrous tetrahydrofuran (10.0 ml, freshly distilled from lithium aluminum hydride) at −78° (Dry Ice) under Ar while a solution of diisobutylaluminum hydride in benzene (0.45 ml, 1.50 *M*, 0.68 mmol) was added dropwise. After 10 min the cooling bath was removed and the clear solution was allowed to stir at room temperature for 22 hr. The reaction mixture was quenched at 0° (ice bath) with 10% hydrochloric acid (1.0 ml), poured into water (50 ml), and extracted with ether (4 × 25 ml). The combined ethereal extracts were washed with water (3 × 50 ml) and saturated sodium chloride solution (50 ml), dried (Na_2SO_4), and concentrated *in vacuo* to give 0.117 g of a colorless oil. Preparative thin layer chromatography on a 20 × 20 cm silica gel plate using 50% ether–50% petroleum ether eluent gave 0.099 g (82%) of white, crystalline ketol **9** (R_f 0.16–0.34): mp 65.5–66° ir ($CHCl_3$) 3600, 3460 (OH), 1725 (CO), 1395, 1389, 1375 cm^{-1} (*gem*-CH_3); nmr ($CDCl_3$) δ 4.37–4.67 (symmetrical multiplet, coupled ABX, 1, $J_{C\text{-}1,C\text{-}8}$ = 2, J_{AB} = 14 Hz, CHOH), 2.95 (s, 1, –OH), 2.50 and 2.27, 1.80 and 1.60 (two doublets, 2, J = 8 Hz, and two doublets, J = 5 Hz, CH_2 at C-7), 1.97 (d, 1, J = 2 Hz, bridgehead at C-1, dihedral angle between protons on C-1 and C-7 must be near 130°), 1.15 (s, 9, $-CH_3$).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.31; H, 10.14.

2-(2′-Propanoic acid)-2,6,6-trimethylcycloheptanone (10).[8,24,27] **Method A.** A mixture of keto olefin **6C** (10.0 g, 45.0 mmol), sodium metaperiodate (48.0 g, 225 mg-atoms), and distilled water (1.0 l.) was stirred until all the sodium metaperiodate dissolved. *tert*-Butyl alcohol (525 ml) was added with stirring and the solution became homogeneous. Catalytic amounts of ruthenium trichloride solution (2 ml, 0.0385 g/ml) and osmium tetroxide solution (10 ml, 0.0025 g/ml) were added. The flask was then filled completely with distilled water, carefully stoppered, and allowed to stir for 188 hr at room temperature. The reaction mixture was poured into water (2 l.) and extracted with ether (10 × 200 ml). The combined ethereal extracts were washed with 10% sodium hydroxide solution (5 × 100 ml). These combined aqueous extracts were washed with ether (100 ml). The aqueous layer was then carefully acidified with cooling (ice bath) with concentrated hydrochloric acid. The slightly acidic aqueous mixture was extracted with ether (5 × 100 ml) and the combined ethereal extracts were washed with water (50 ml) and saturated sodium chloride solution (50 ml), dried ($MgSO_4$), and concentrated *in vacuo* to give 9.46 g (93%) of pale yellow, crystalline keto acid **10:** mp 125–125.5°; ir ($CHCl_3$) 2400–3580 (CO_2H), 1710, 1700 (CO_2H, CO), 1380, 1370 cm^{-1} (*gem*-CH_3); nmr (CCl_4) δ 8.05 (bs, 1, CO_2H), 3.49 (distorted AB, 3, J_{AB} = 7 Hz, CHCO and $COCH_2$), 1.18 (s, 3, CH_3), 1.04 (bs, 6, *gem*-CH_3), and 0.90 ppm (d, 3, J = 5.6 Hz, CH_3CH).

Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.81; H, 9.70.

3,3,7,8-Tetramethyl-9-oxo-10-oxabicyclo[5.3.0]dec-1-ene (11).[28] **Method A.** A solution of keto acid **10** (13.3 g, 58.9 mmol) and anhydrous sodium acetate (0.274 g) in acetic anhydride (50 ml) was stirred at reflux for 5 hr. After cooling to room temperature the orange-brown mixture was poured into ether (250 ml). This ethereal solution was washed with water (3 × 50 ml), 5% disodium hydrogen phosphate solution (3 × 25 ml), and saturated sodium chloride solution (3 × 50 ml), and dried overnight (Na_2SO_4) containing methanol (150 ml) and pyridine (0.5 ml). The resulting mixture was filtered and concentrated *in vacuo* to give 11.6 g (95%) of a red oil. Distillation gave 10.6 g (87%) of colorless liquid enol lactone **11,** bp 86–89° (0.4 mm).

Method B.[31] A solution of keto acid **10** (16.5 g, 72.9 mmol) and acetic anhydride (20.0 ml, 212 mmol, freshly distilled), in anhydrous dichloromethane (400 ml, freshly distilled from phosphorous pentoxide) containing 60% perchloric acid (20 μl) was allowed to stir at room temperature for 4 hr. The reaction mixture was washed with water (3 × 100 ml), saturated sodium bicarbonate solution (100 ml) and water (100 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The last traces of acetic anhydride were removed with methanol (50 ml) containing a trace of pyridine (0.2 ml) and again concentrated *in vacuo* to give 14.8 g (97.4%) of an orange oil. Distillation gave 13.7 g (90%) of colorless liquid enol lactone **11:** bp 86–89° (0.4 mm); ir (film) 3040 (OC=CH), 1790 (CO), 1685 (OC=CH), 1390, 1375 (*gem*-CH_3), 855 and 841 cm^{-1} (OC=CH); nmr (CCl_4) δ 5.19 (m, 1, OC=CH), 1.30 (s, 3, CH_3), and 1.10 ppm (s, 6, *gem*-CH_3); glc analysis on column D shows the product to be a 70:30 mixture of diastereomers (column temperature 145°, retention times 7.2 and 9.1 min).

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.91; H, 9.72.

2,2,6,7-Tetramethyl-8-*exo*-hydroxybicyclo[4.2.1]nonan-9-one (12).[28] A solution of enol lactone **11** (1.796 g, 8.62 mmol) in anhydrous tetrahydrofuran (80 ml, freshly distilled from lithium aluminun hydride) was stirred under nitrogen at −78° (Dry Ice) while a benzene solution of diisobutylaluminum hydride (6.00 ml, 1.50 *M*, 9.0 mmol) was added dropwise. After 30 min the cooling bath was removed and the clear solution was allowed to stir at 60° (bath temperature) for 18 hr. The reaction mixture was cooled to room temperature and poured into an ice–water mixture (200 ml) containing 10% hydrochloric acid (6 ml). The mixture was extracted with ether (6 × 50 ml). The combined ethereal extracts were washed with water (4 × 100 ml) and saturated sodium chloride solution (100 ml), dried (Na_2SO_4), and concentrated *in vacuo* to give 1.90 g of crude oil. The crude product was immediately chromatographed on silica gel (190 g, 75–325 mesh, E. Merck) in a 2.5-cm diameter column. A 50:50 mixture of ether and petroleum ether was used to develop the column, taking 80-ml sized fractions. Fractions 7–11 gave 1.45 g (80%) of pure ketol **12** as a colorless liquid. Analysis by glc on column D showed the ketol **12** to be a 66:34 mixture of diastereomers: bp 105° (0.2 mm, bulb to bulb, external temperature); ir (film) 3440 (–OH), 1725 cm^{-1} (CO). This compound was found to be very sensitive to acid- or base-catalyzed fragmentation and was immediately carried on to the next reaction.

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.25; H, 10.65.

2,2,6,7-Tetramethylbicyclo[4.2.1]non-7-en-9-one (13).[32,33] A solution of ketol **12** (1.835 g, 8.72 mmol) in anhydrous dichloromethane (60 ml, freshly distilled from phosphorus pentoxide) was stirred at 0° (ice bath) while triethylamine (1.337 g, 13.2 mmol, freshly distilled from calcium hydride) and methanesulfonyl chloride (1.105 g, 9.05 mmol, freshly distilled) were added sequentially. The resulting pale yellow solution was stored in a refrigerator at 3° for 17 hr. The solution was transferred to a separatory funnel with dichloromethane (600 ml) and water (150 ml). The organic layer was separated, washed with water (150 ml), 5% hydrochloric acid (150 ml), and saturated sodium chloride solution (150 ml), dried (Na_2SO_4), and concentrated *in vacuo* to give 2.52 g of a crude oil. This oil was dissolved in collidine (55 ml, dried over barium oxide). After stirring under nitrogen at 170–175° (bath temperature) for 16 hr, the dark brown solution was cooled to room temperature and diluted with ether (500 ml) and water (150 ml). The ether layer was separated, washed with 5% hydrochloric acid (6 × 150 ml), water (150 ml), saturated sodium bicarbonate solution (150 ml), water (150 ml), and saturated sodium chloride solution (150 ml), dried (Na_2SO_4), and concentrated *in vacuo* to give 1.66 g of crude ketone **13.** Distillation gave 1.46 g (87%) of pure ketone **13:** bp 46° (0.2 mm, external temperature); ir ($CHCl_3$) 1735 (CO),

1645, 850 cm^{-1} (C=CH) [lit.[34] ir ($CHCl_3$) 1738, 1650, 850 cm^{-1}]; nmr (CCl_4) δ 5.80 (q, 1, J = 2 Hz, CH=C), 2.35 (q, 1, J = 2 Hz, bridgehead at C-1), 1.66 (t, 3, J = 2 Hz, CH_3C=CH), 1.04 (s, 6, CH_3), 0.97 ppm (s, 3, CH_3).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 80.97; H, 10.52.

2,2,6,7-Tetramethyl-9-methoxymethylenebicyclo[4.2.1]non-7-ene (14).[35] Sodium hydride (1.288 g of a 57% dispersion in oil, 30.6 mg-atoms) was washed with anhydrous ether (3 × 20 ml, freshly distilled from lithium aluminum hydride) under nitrogen. The remaining traces of ether were removed by warming the sodium hydride in a stream of dry nitrogen. After cooling to room temperature dimethyl sulfoxide (85 ml, freshly vacuum distilled from calcium hydride) was added. The mixture was stirred under nitrogen at 50–60° (bath temperature) for 2.75 hr. After the solution was cooled to room temperature methoxymethyltriphenylphosphonium chloride (10.42 g, 30.42 mmol) was added. The resulting deep red solution was stirred for 15 min, and then enone **13** (2.94 g, 15.6 mmol) dissolved in dry dimethyl sulfoxide (3 × 5.0 ml, freshly vacuum distilled from calcium hydride) was added. The resulting reaction mixture was stirred at 59° ± 2° (bath temperature) for 23.5 hr. The orange solution was cooled to room temperature and poured into water (500 ml) and ether (500 ml). The aqueous layer was separated and extracted further with ether (3 × 250 ml). The combined ethereal extracts were washed with 10% hydrochloric acid (200 ml), water (10 × 200 ml), and saturated sodium chloride solution (200 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The resulting concentrate (7.45 g) was dissolved in petroleum ether (10 ml) and allowed to stand overnight. The liquid was separated from the crystalline triphenylphosphine oxide and concentrated *in vacuo* to give 4.10 g of crude product. This crude liquid was chromatographed on silica gel (400 g, 75–325 mesh) in a 4.0-cm diameter column using a 2.5% ether–97.5% petroleum ether solution to develop the column, taking 200-ml sized fractions. Fractions 4–6 were concentrated and distilled to give 2.97 g (88%) of pure methoxyvinyl ether **14**: bp 45 ± 2° (0.2 mm, external temperature); ir (film) 3070 (C=CH), 1695 (C=CO), 1385 and 1365 cm^{-1} (*gem*-CH_3); nmr (CCl_4) δ 5.64 (m, 1, C=CHO), 5.4 (m, 1, CH=C), 3.5 (s, 3, CH_3O), 2.92 (m, 1, bridgehead H), 1.57 (m, 3, CH_3C=C), 1.01 (s, 3, CH_3), 0.92 (s, 3, CH_3), and 0.82 ppm (s, 3, CH_3).

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.79; H, 10.82.

2,2,6,7-Tetramethylbicyclo[4.2.1]non-7-ene-9-*exo*-carboxaldehyde (15).[35] Perchloric acid (20 ml, 50%) was slowly added to a solution of methoxyvinyl ether **14** (1.477 g, 6.7 mmol) in ether (100 ml) under nitrogen. The resulting homogeneous solution was stirred for 1.75 hr at room temperature and then poured into pentane (100 ml) and water (100 ml). The aqueous layer was separated and extracted with pentane (4 × 50 ml). The combined organic extracts were washed with water (50 ml) and saturated sodium chloride solution (50 ml), dried (Na_2SO_4), and concentrated *in vacuo*. The crude aldehyde was dissolved in dry methanol (100 ml) containing anhydrous potassium carbonate (1.0 g). The slurry was stirred at room temperature for 1.75 hr under nitrogen and then poured into water (100 ml). This aqueous solution was extracted with pentane (6 × 40 ml). The combined pentane extracts were washed with water (40 ml) and saturated sodium chloride solution (40 ml), dried (Na_2SO_4), and concentrated *in vacuo*. Distillation gave 1.40 g (100%) of pure aldehyde **15**: bp 45 ± 2° (0.2 mm, external temperature); ir (CCl_4) 3060 (C=CH), 2745 (-CHO), 1720 (CO), 1385, and 1365 cm^{-1} (*gem*-CH_3); nmr (CCl_4) δ 9.32 (d, 1, J = 7 Hz, -CHO), 5.42 (m, 1, C=CH), 2.35 (d, 1, J = 7 Hz, OCCH), 2.11 (m, 1, bridgehead H), 1.55 (m, 3, CH_3C=C), 1.03 (s, 3, CH_3), and 0.93 ppm (s, 6, CH_3).

Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.38; H, 10.70.

2,2,6,7-Tetramethylbicyclo[4.2.1]non-7-ene-9-*exo*-carboxylic Acid (16).[36,37] Jones reagent (2.5 ml, 2.67 *M*, 6.67 mmol) was added dropwise to a solution of aldehyde **15** (1.25 g, 6.06 mmol) dissolved in anhydrous acetone (50 ml, dried over magnesium sulfate) at 0° (ice bath) with vigorous stirring. The ice bath was removed after the addition and after 30 min the reaction was quenched with reagent isopropyl alcohol (enough to remove the orange color). The reaction mixture was dissolved in water (150 ml) and extracted with ether (10 × 25 ml). The combined ethereal extracts were washed with water (25 ml) and then with 10% sodium hydroxide solution (5 × 50 ml). The basic extracts were carefully acidified with concentrated hydrochloric acid while cooling in an ice bath. This acidified solution was extracted with ether (5 × 50 ml). The combined ethereal extracts were washed with water (25 ml) and saturated sodium chloride solution (25 ml), dried (Na_2SO_4), and concentrated *in vacuo* to give 1.15 g (86%) of acid **16**. A small sample of this acid was recrystallized from pentane (three times) to give pure acid **16**: mp 127.5–128°; ir (CCl_4) 3060 (-CO_2H), and 1700 cm^{-1} (CO); nmr (CCl_4) δ 11.47 (s, 1, -CO_2H), 5.43 (m, 1, C=CH), 2.68 (s, 1, $CHCO_2H$), 2.37 (m, 1, bridgehead H), 1.52 (m, 3, CH_3C=C), 1.12 (s, 3, CH_3), 0.93 (s, 3, CH_3), and 0.88 ppm (s, 3, CH_3).

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.62; H, 9.91.

2,2,6,10-Tetramethyltetracyclo[5.4.0.0^{6,10}.0^{9,11}]undecan-8-one (17).[38] A solution of the olefinic acid **16** (0.499 g, 2.25 mmol) dissolved in benzene (20 ml, freshly distilled from calcium hydride) was stirred at 0° (ice bath) under nitrogen while oxalyl chloride (1.35 ml, 2.0 g, 15.75 mmol) was added dropwise. The ice bath was removed and the solution was stirred at room temperature for 2 hr. The solvent and excess reagent were removed *in vacuo*. The resulting orange oil was dissolved in benzene (2 × 5.0 ml, freshly distilled from calcium hydride) under nitrogen. This solution was added dropwise at 0° (ice bath) to an anhydrous ethereal solution of diazomethane (50 ml, ~20 mmol, predried over sodium metal) with vigorous stirring under nitrogen. The resulting solution was stirred at 0° for 1 hr and then at room temperature for 1.5 hr. The solvents and excess reagent were removed *in vacuo*. Tetrahydrofuran (40 ml, freshly distilled from lithium aluminum hydride) and finely divided metalic copper powder (0.67 g, Fischer C-434) were added to the crude diazo ketone, sequentially. This suspension was vigorously stirred at reflux under nitrogen for 2 hr. The resulting suspension was allowed to stir at room temperature for an additional 14 hr. The solution was filtered into water (100 ml). The mixture was shaken vigorously for 5 min and then extracted with ether (3 × 50 ml). The combined ethereal extracts were washed with saturated sodium bicarbonate solution (4 × 40 ml), water (40 ml), and saturated sodium chloride solution (40 ml), dried (Na_2SO_4), and concentrated *in vacuo* to give 0.673 g of a crude brown oil. This crude oil was chromatographed on silica gel (67 g, 75–325 mesh, E. Merck) in a 2-cm diameter column using 10% ether–90% petroleum ether to develop the column, taking 37-ml sized fractions. Fractions 11–16 gave 0.164 g (33%) of pure ketone **17**: mp 64–64.5° (from pentane); ir (CCl_4) 3095 (cyclopropyl CH) and 1755 cm^{-1} (CO); nmr (CCl_4) δ 1.18 (s, 3, CH_3) 1.03 (s, 3, CH_3), 0.97 (s, 3, CH_3), and 0.90 ppm (s, 3, CH_3).

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.61; H, 10.01.

2,2,6,10-Tetramethyltetracyclo[5.4.0.0^{6,10}.0^{9,11}]undecan-8β-ol (18). Diisobutylaluminum hydride in benzene (0.65 ml, 1.26 *M*, 0182 mmol) was added to a stirred solution of tetracyclic ketone **17** (0.164 g, 0.75 mmol) in anhydrous tetrahydrofuran (15 ml, freshly distilled from lithium aluminum hydride) at −78° (Dry Ice) under nitrogen. The resulting solution was stirred at −78° for 30 min, at 0° for 30 min, and at room temperature for 3 hr. The solution was then poured into a mixture of ice and 10% sodium hydroxide solution (25 g:25 ml). The mixture was extracted with ether (6 × 30 ml). The combined ethereal extracts were washed with water (3 × 30 ml) and saturated sodium chloride solution (30 ml), dried (Na_2SO_4), and concentrated *in vacuo* to give 0.169 g of crude crystalline alcohol **18**. Recrystallization from pentane (once) gave 0.162 g (98%) of pure alcohol **18**: mp 114–115°; ir (CCl_4) 3650 (free OH), 3325 (H-bonded OH), 3075 (cyclopropyl CH), 1380, and 1365 cm^{-1} (*gem*-CH_3); nmr (CCl_4) δ 3.63 (s, 1, CHO), 1.73 (s, 1, OH), 1.20 (s, 3, CH_3), 1.05 (s, 3, CH_3), 0.92 (s, 3, CH_3), and 0.87 ppm (s, 3, CH_3).

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.80; H, 10.93.

(±)-Longicyclene (1).[9] To a stirred solution of tetracyclic alcohol **18** (0.1375 g, 0.625 mmol) in anhydrous dichloromethane (5.0 ml, freshly distilled from phosphorus pentoxide) at 0° (ice bath) under nitrogen were added sequentially triethylamine (0.13 g, 0.180 ml, 1.27 mmol, freshly distilled from calcium hydride) and methanesulfonyl chloride (0.147 g, 0.097 ml, 1.28 mmol, freshly distilled). The solution was stored in a freezer at −15° for 72 hr.[32] The reaction mixture was then poured into a mixture of lithium aluminum hydride (0.2033 g, 5.35 mg-atoms) and ether (20 ml, freshly distilled from lithium aluminum hydride). This mixture was stirred at reflux for 7.5 hr and left to stir at room temperature for 9.5 hr. The reaction mixture was poured into ice–10% sodium hydroxide solution (30 g:30 ml) and extracted with ether (5 × 30 ml). The combined ethereal extracts were washed with 10% hydrochloric acid (30 ml), saturated sodium bicarbonate solution (30 ml), water (2 × 30 ml), and saturated sodium chloride solution, dried (Na_2SO_4), and concentrated carefully *in vacuo* at room tem-

Table I

Column	Column temp, °C	Retention time, min
B	100	17.1
C	110	15.4
D	100	12.9
E	100	11.3
F	110	18.7

perature to give 0.136 g of crude (±)-longicyclene (1). The crude product was chromatographed on silica gel (10 g, 75–325 mesh, E. Merck) in a 1-cm diameter column using pentane to develop the column, taking 5-ml sized fractions. Frations 3–5 gave after distillation 0.125 g (98%) of pure (±)-longicyclene (1): bp 82° (2.0 mm, external temperature); ir (CCl_4) 3085 (cyclopropyl H), 1385, and 1370 cm^{-1} (*gem*-CH_3); nmr (CCl_4) δ 1.04 (s, 3, CH_3), 0.98 (s, 3, CH_3), 0.92 (s, 3, CH_3), and 0.88 ppm (s, 3, CH_3). The spectral data are identical with those for natural (+)-longicyclene.[9]

Synthetic (±)-longicyclene was found to have identical retention times with those of natural (+)-longicyclene[9] on glc both in separate and coinjected samples using columns B–F. Glc data on separate and coinjected samples of longicyclene are listed in Table I.

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.28; H, 11.78.

2,2,6,7-Tetramethyl-9-*exo*-vinylbicyclo[4.2.1]non-7-ene (19).[43] Sodium hydride (0.0840 g, 2.00 mg-atoms) of a 57% dispersion in oil was washed under nitrogen with anhydrous ether (3 × 2 ml, freshly distilled from lithium aluminum hydride) and the last traces of ether were removed by warming the sodium hydride in a stream of nitrogen. After cooling to room temperature, dry dimethyl sulfoxide (11 ml, freshly distilled from calcium hydride) was added and the mixture was stirred under nitrogen at 60 ± 2° until the evolution of hydrogen ceased. The resulting clear solution was cooled to room temperature and methyltriphenylphosphonium bromide (0.715 g, 2.00 mmol) was added. The yellow solution was stirred at room temperature for 15 min, and then aldehyde **15** (0.1961 g, 0.95 mmol) was added. The reaction mixture was allowed to stir at room temperature for 13.5 hr. The orange solution was poured into water (60 ml) and extracted with pentane (5 × 30 ml). The combined pentane extracts were washed with 10% hydrochloric acid solution (20 ml), saturated sodium bicarbonate solution (20 ml), water (20 ml), and saturated sodium chloride solution, dried (Na_2SO_4), and concentrated to approximately 10 ml *in vacuo* at room temperature. This solution was chromatographed on silica gel (20 g, 75–325 mesh, E. Merck) in a 1.5-cm diameter column using pentane to develop the column, taking 10-ml sized fractions. Fractions 5 and 6 gave after concentration and distillation 0.1603 g (83%) of pure diene **19**: bp 125° (30 mm, external temperature); ir (CCl_4) 3060 (C=CH, H_2C=CH), 1660 (C=CH), 1635 (H_2C=CH), 1385, 1375 (*gem*-CH_3), and 905 cm^{-1} (H_2C=CH); nmr (CCl_4) δ 5.3–6.0 (m, 2, H_2C=C**H** and C=CH), 4.88 (doublet of doublets, 1, J = 11 and 2.5 Hz, cis proton to R in $\mathbf{H_2C}$=CHR), 4.67 (overlapping doublet of doublets, 1, trans proton to R in $\mathbf{H_2C}$=CHR), 2.38 (d, 1, J = 9.5 Hz, H_2C=CHC**H**), 1.85 (m, 1, bridgehead H), 1.57 (t, 3, $\mathbf{CH_3}$C=CH), 0.97 (s, 3, CH_3), 0.95 (s, 3, CH_3), and 0.93 ppm (s, 3, CH_3).

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.22; H, 11.85.

2,2,6,*endo*-7-Tetramethyl-9-*exo*-(2′-hydroxyethyl)bicyclo[4.2.1]nonan-*exo*-8-ol (20). Method A.[43] Diborane–tetrahydrofuran solution (2.3 ml, 0.75 *M*, 1.73 mmol, Alfa Inorganics) was added to a stirred solution of diene **19** (88.3 mg, 0.432 mmol) in anhydrous tetrahydrofuran (4.0 ml), freshly distilled from lithium aluminum hydride) at 0° (ice bath) under nitrogen. The resulting solution was allowed to stir at room temperature for 3 hr. The solution was cooled to 0° (ice bath) and a mixture of 30% hydrogen peroxide and 10% sodium hydroxide solution (5 ml:5 ml) was added dropwise. The reaction mixture was stirred vigorously at 0° (ice bath) for 1 hr and then stirred at room temperature for 1 hr. The solution was poured into water (50 ml) and extracted with ether (5 × 20 ml). The combined ethereal extracts were waawashed with 10% sodium hydroxide solution (10 ml) and saturated sodium chloride solution (2 × 10 ml), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was chromatographed on silica gel (10 g, 70–230 mesh, E. Merck) in a 1-cm diameter column using 25% acetone–75% petroleum ether to develop the column, taking 5-ml sized fractions. Fractions 13–17 gave 0.0509 g (49%) of pure diol **20**, mp 130.5–131°.

Method B.[43] Diborane–tetrahydrofuran solution (30 ml, 0.75 *M*, 20.4 mmol, Alfa Inorganics) was added to a stirred solution of 2-methyl-2-butene (3.14 g, 44.8 mmol, distilled from sodium metal) in anhydrous tetrahydrofuran (30 ml, freshly distilled from lithium aluminum hydride) at 0° (ice bath) under nitrogen. The ice bath was removed and the solution was allowed to stir at room temperature for 3 hr and then recooled to 0° (ice bath). A solution of diene **19** (0.8324 g, 4.07 mmol) in dry tetrahydrofuran (5.0 ml, freshly distilled from lithium aluminum hydride) was added. The resulting solution was allowed to stir at room temperature for 11.3 hr and then cooled to 0° (ice bath) and carefully quenched with distilled water (3 ml). This was immediately followed by a mixture of 30% hydrogen peroxide and 10% sodium hydroxide solution (50 ml:50 ml). The resulting reaction mixture was stirred vigorously at 0° (ice bath) for 3 hr and then stirred at room temperature for 3 hr. The mixture was poured into water (400 ml) and extracted with ether (6 × 75 ml). The combined ethereal extracts were washed with 10% sodium hydroxide solution (50 ml), water (3 × 50 ml), and saturated sodium chloride solution (50 ml), dried (Na_2SO_4), and concentrated *in vacuo*. Excess isoamyl alcohol was removed under high vacuum. The crude product (1.58 g) was chromatographed on silica gel (158 g, 70–230 mesh) in a 2.5-cm diameter column using 25% acetone–75% petroleum ether solution to develop the column, taking 75-ml sized fractions. Fractions 14–18 gave 0.478 (49%) of diol **20**, mp 130–131°. Recrystallization of a small sample from ether–hexane (once) gave analytically pure diol **20**: mp 130.5–131°; ir ($CHCl_3$) 3625 (free OH), 3400 (H-bonded OH), 1385, and 1370 cm^{-1} (*gem*-CH_3); nmr ($CDCl_3$) δ 4.04 (doublet of doublets, an X part of an AMX system, 1, first-order analysis $J_{7,8}$ = 7.8 and $J_{1,8}$ = 2.6 Hz, RC**H**OHR′), 3.9–3.5 (m, 2, C$\mathbf{H_2}$OH), 2.03 (s, 2, OH), 1.03 (s, 3, CH_3), 0.93 (s, 3, CH_3), and 0.90 ppm (s, 6, CH_3).

Anal. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.84; H, 11.71.

2,2,6*endo*-7-Tetramethyl-9-*exo*-(2′-ethyl methanesulfonate)bicyclo[4.2.1]nonan-8-one (21).[32,46,47] Triethylamine (0.046 g, 0.454 mmol, freshly distilled from calcium hydride) and methanesulfonyl chloride (0.0596 g, 0.433 mmol) were sequentially added to a stirred solution of diol **20** (0.0994 g, 0.413 mmol) in anhydrous dichloromethane (6.0 ml, freshly distilled from phosphorus pentoxide) at 0° (ice bath) under nitrogen. The reaction was monitored by tlc (silica gel) using 50% acetone–50% petroleum ether to develop the plates [R_f (product) 0.66, R_f (starting material) 0.59]. After 36 hr at 3° (refrigerator) the solution was diluted with dichloromethane (40 ml), washed with water (2 × 10 ml), 5% hydrochloric acid (10 ml), saturated sodium bicarbonate solution (10 ml), and water (10 ml), dried (Na_2SO_4), and concentrated *in vacuo* to give 0.1286 g (97.4%) of a crude liquid hydroxy mesylate: ir (CCl_4) 3400 (OH), 1370, and 1180 cm^{-1} (CH_3SO_2OR); nmr (CCl_4) δ 4.37–3.77 (m, 3, C**H**OH and $\mathbf{CH_2}$OMs), 2.93 (s, 3, CH_3SO_3–), 2.50 (s, 1, OH), 1.03 (((s, 3, CH_3), 0.94 (s, 3, CH_3), and 0.90 (s, 6, CH_3). This material was used immediately in the next step without further purification.

To a solution of dry pyridine (0.4465 g, 5.65 mmol, freshly distilled from calcium hydride) in anhydrous dichloromethane (5.0 ml, freshly distilled from phosphorus pentoxide) at 0° (ice bath) under nitrogen was added chromium trioxide (0.282 g, 2.82 mg-atoms, Alfa Inorganics No. 87844, dried in a desiccator over phosphorus pentoxide). The burgundy solution was stirred at 0° for 5 min and then at room temperature for 10 min. A solution of the crude hydroxy mesylate (0.1286 g, 0.403 mmol) in dry dichloromethane (1.0 ml) was added quickly. A heavy, black, tarry residue separated immediately. After stirring for 15 min the brown-black solution was filtered through a column of Woelm neutral alumina (10 g, in a 1-cm diameter column, activity III) using dichloromethane (4 × 25 ml) to elute. The combined colorless eluent was concentrated *in vacuo* to give 0.121 g (92% overall) of keto mesylate **21**: mp 126–127°; tlc (silica gel) using 20% ether–80% petroleum ether to develop the plate shows only one spot. A small sample was recrystallized from pentane to give analytically pure keto mesylate **21**: mp 126–127°; ir ($CHCl_3$) 1725 (CO), 1370 and 1180 cm^{-1} (CH_3SO_2OR); nmr ($CDCl_3$) δ 4.5–4.1 (m, 2, C$\mathbf{H_2}$OMs), 3.0 (s, 3, CH_3SO_3) 1.10 (s, 3, CH_3), 1.06 (s, 3, CH_3), 1.00 (s, 3, CH_3), and 0.97 ppm (d, 3, J = 7 Hz, $\mathbf{CH_3}$CH).

Anal. Calcd for $C_{16}H_{28}O_4S$: C, 60.65; H, 8.92; S, 10.22. Found: C, 60.72; H, 8.92; S, 10.13.

(±)-Longicamphor (2A).[48] A solution of sodium bis(trimethylsilyl)amide in benzene (0.33 ml, 0.97 *M*, 0.32 mmol) was added dropwise to a stirred solution of keto mesylate **21** (99.4 mg, 0.314 mmol) dissolved in anhydrous 1,2-dimethoxyethane (5.0 ml, freshly distilled from lithium aluminum hydride) under nitrogen

Table II

Column	Column temp, °C	Retention time, min
B	220	12.3
C	170	15.0
D	120	12.0
E	170	13.2
F	190	11.2

Table III

Column	Column temp, °C	Retention time, min
B	200	14.2
C	190	17.6
D	120	13.5
E	170	13.0
F	170	13.5

at 0° (ice bath). The solution turned yellow, the ice bath was removed, and the solution was stirred at room temperature for 40 min. The yellow solution was diluted with ether (50 ml), washed with water (10 ml), 10% hydrochloric acid (2 × 10 ml), saturated sodium bicarbonate solution (2 × 10 ml), water (10 ml), and saturated sodium chloride solution (10 ml), dried (Na_2SO_4), concentrated *in vacuo*, and distilled to give 68.0 mg (98%) of pure (±)-longicamphor (**2A**): bp 50° (20 mm, external temperature); ir (CCl_4) 1735 (CO), 1390, and 1375 cm^{-1} (*gem*-CH_3); nmr (CCl_4) δ 1.60 (s, 1, bridgehead H), 1.13 (s, 3, CH_3CCO), 0.92 (s, 3, CH_3), and 0.87 ppm (s, 6, $-CH_3$). The spectral data are identical with those observed for natural (+)-longicamphor.

Synthetic (±)-longicamphor was found to have identical retention times with those of natural (+)-longicamphor[10,13,14] on glc both in separate and coinjected samples using columns B–F. Glc data on separate and coinjected samples of longicamphor are listed in Table II.

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.84; H, 11.08.

(±)-Longiborneol (2B).[34,49] Racemic longicamphor (**1**, 67 mg, 0.304 mmol) was added to a blue solution of calcium metal (120 mg) in liquid ammonia (30 ml, distilled through potassium hydroxide towers). 1-Propanol was immediately added dropwise until the blue color was dispelled. The ammonia was evaporated and the residue was taken up in water (100 ml) and ether (100 ml). The aqueous layer was separated and extracted with ether (3 × 25 ml). The combined ethereal extracts were washed with water (5 × 10 ml) and saturated sodium chloride solution (20 ml), dried (Na_2SO_4), and concentrated *in vacuo*. The excess 1-propanol was removed under high vacuum. The crude product was recrystallized from pentane (once) to give 65.5 mg (97%) of pure (±)-longiborneol (**2b**): mp 100–102°; ir (CCl_4) 3640 (free OH), 3450 (H-bonded OH), 1370, 1385 (*gem*-CH_3), and 1050 cm^{-1} (COH); nmr (CCl_4) δ 3.68 (d, 1, J = 6 Hz, CHOH), 0.93 (s, 6, $-CH_3$), and 0.85 ppm (s, 6, CH_3). The spectral data are identical with those observed for natural (+)-longiborneol.

Synthetic (±)-longiborneol was found to have identical retention times with those of natural (+)-longiborneol[10,13,14] on glc both in separate and coinjected samples using columns B–F. Glc data on separate and coinjected samples of longiborneol are listed in Table III.

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.01; H, 11.77.

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Registry No.—**1**, 41437-68-7; **2A**, 51868-75-8; **2B**, 51897-51-9; **3**, 2244-16-8; **4**, 503-93-5; **5**, 4436-59-3; **6A**, 51830-59-2; **6B**, 51830-60-5; **6C**, 51830-61-6; **6D**, 51830-62-7; **7A**, 51830-63-8; **7B**, 51830-64-9; **8**, 51830-65-0; **9**, 51830-67-2; **10**, 51830-66-1; **11** epimer A, 51868-76-9; **11** epimer B, 51868-77-0; **12** epimer A, 51868-78-1; **12** epimer B, 51868-79-2; **13**, 41509-35-7; **14**, 51830-68-3; **15**, 41435-94-3; **16**, 41437-67-6; **17**, 41509-36-8; **18**, 51830-69-4; **19**, 51830-70-7; **20**, 51830-71-8; **20** mesylate, 51830-72-9; **21**, 51830-73-0; allyl bromide, 106-95-6; ethyl 2-bromoacetate, 105-36-2; *trans*-3-penten-2-ol, 3899-34-1; crotonaldehyde, 4170-30-3; *trans*-4-chloro-2-pentene, 18610-33-8; ethyl 2-bromopropanoate, 535-11-5.

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