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Relative Configurations of the Chiral 2,7- and 3,7-Dimethyl-7-(methoxymethyl)cyclohepta-1,3,5-trienes

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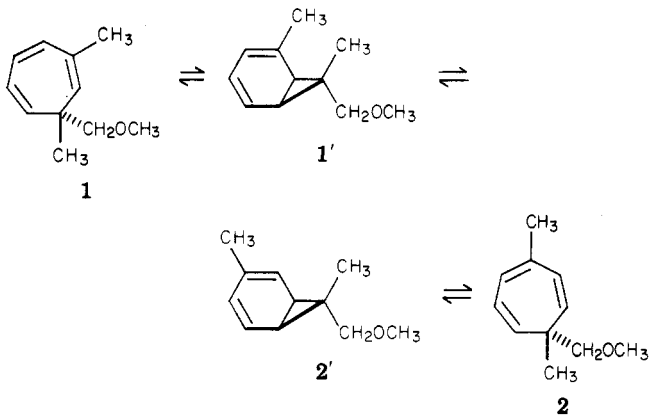
A chiral sample of 5-(methoxymethyl)-5-methylcyclohept-2-en-1-one was synthesized and converted in two separate reaction sequences to 2,7- and 3,7-dimethyl-7-(methoxymethyl)cycloheptatriene. The synthetic chemistry and the observed rotations of the cycloheptatriene products demonstrate that the isomers exhibit the same sign of rotation at 436 nm when they have different *R,S* designators of absolute stereochemistry. These assignments of relative stereochemistry for 2,7- and 3,7-dimethyl-7-(methoxymethyl)cycloheptatriene confirm the relative stereochemical assignments and the reaction stereochemistry inference reached by Klärner and Brassel: the thermal isomerization of 2,7-dimethyl-7-(methoxymethyl)cycloheptatriene to the 3,7 isomer occurs predominantly with inversion at the migrating carbon in the norcaradiene form.

In 1980 Klärner and Brassel reported that chiral 2,7-dimethyl-7-(methoxymethyl)cyclohepta-1,3,5-triene (**1**)



isomerized at 220 °C to give 3,7-dimethyl-7-(methoxymethyl)cycloheptatriene (**2**) of somewhat diminished optical purity and of opposite sign of rotation.[1] The isomeric cycloheptatrienes were related configurationally to the corresponding 2,7- and 3,7-dimethyl-7-(methoxycarbonyl)cycloheptatrienes, compounds of previously assigned relative stereochemistry,[2] and the reaction stereochemistry was deduced: the [1,5] carbon migration in the norcaradiene form of 2,7-dimethyl-7-(methoxymethyl)-cycloheptatriene occurred with predominant inversion at the migrating carbon atom. Thus the *R* isomer of **1** rearranges to the *R* form of the product or the *S* substrate to the (*S*)-3,7-dimethyl compound, with a change in the sign of rotation.

These stereochemical findings seemed to conflict with our preliminary report on the stereochemical course of a closely related isomerization, the degenerate rearrangement of (+)-2-deuterio-3,7-dimethyl-7-(methoxymethyl)cycloheptatriene,[3] and we scrutinized our own work and Klärner's papers[1,2] most closely in efforts to identify some cause for the inconsistency. When these efforts proved unavailing, further experimental work was undertaken to confirm or to find some error in one or the other investigation.

The relative stereochemistry of the chiral 2,7- and 3,7-dimethyl-7-(methoxycarbonyl)cycloheptatrienes was derived by Klärner with the aid of two thermolyses.[2] First, a 3-g sample of (−)-2,7-dimethyl-7-(methoxycarbonyl)-cycloheptatriene, $[\alpha]_{579}$ −191° (neat), was heated 5 h at 180 °C; the thermolysis mixture was separated to provide 0.35 g of the 3,7-dimethyl isomer, $[\alpha]_{579}$ −4.6° (neat), and 45 mg of optically active methyl α-(3-methylcyclohexa-2,5-dien-1-yl)acrylate (**3**). This dihydrobenzene derivative proved very sensitive to air, being oxidized readily to the corresponding styrene derivative; it was isolated by HPLC and by preparative gas chromatography and was then immediately thermolyzed for 381 min at 180 °C. Spectral and rotational data for **3** were not reported.[2] The 2,7- and 3,7-dimethyl-7-(methoxycarbonyl)cycloheptatrienes **4** and **5** isolated from the second thermolysis reaction mixture were found with the aid of a chiral NMR europium shift reagent to be the (−) antipodes, of 90% and 48% optical

(1) Klärner, F.-G.; Brassel, B. *J. Am. Chem. Soc.* **1980**, *102*, 2469–2470.
(2) Klärner, F.-G.; Yaslak, S.; Wette, M. *Chem. Ber.* **1979**, *112*, 1168–1188.
(3) Baldwin, J. E.; Broline, B. M. *J. Am. Chem. Soc.* **1978**, *100*, 4599–4600. For a full account of this work, see: Baldwin, J. E.; Broline, B. M. *Ibid.*, in press.

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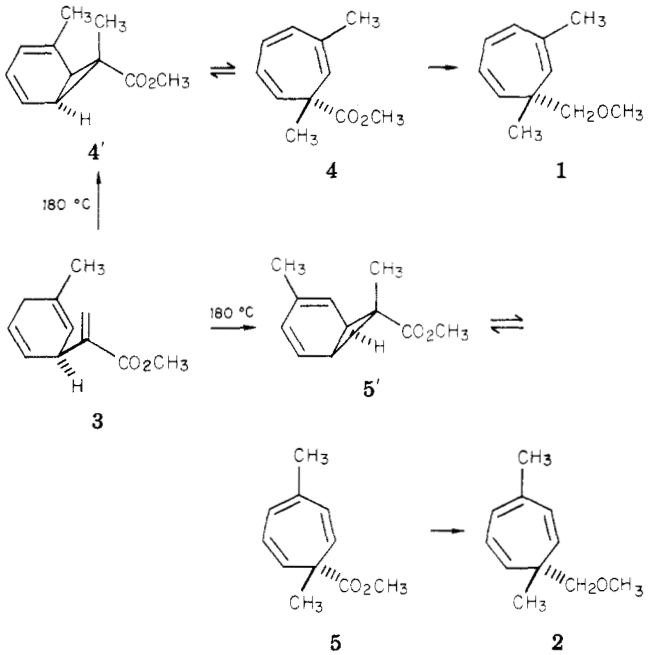
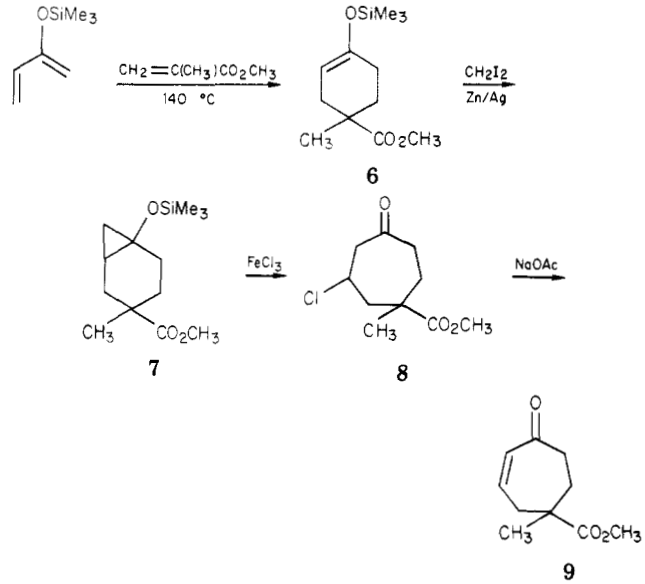
Scheme I



Scheme II



purity, respectively. The logical structure behind this assignment of relatively stereochemistry is apparent from Scheme I.

A [1,5] homodienyl hydrogen shift in the dihydrobenzene system may occur in two ways, but the stereochemistry at C(7) in the cycloheptatriene product must be the same in both. Conversion of these esters to the corresponding 7-methoxymethyl compounds by lithium aluminum hydride reduction followed by methylation with sodium hydride and methyl iodide gave the (−) antipode of the 2,7-dimethyl compound and the (+) enantiomer of 3,7-dimethyl-7-(methoxymethyl)cycloheptatriene.[1]

For this assignment to be totally secure, one would need assurance that the 45 mg of chiral dihydrobenzene derivative **3** isolated from the first thermolysis mixture by a combination of HPLC and gas chromatographic techniques was not contaminated by (−)-**4** or (−)-**5** and that (−)-**4** and (−)-**5** in the second thermolysis reaction mixture were kinetically controlled products from **3** itself.

Two somewhat different estimates of rate constants for the isomerizations in question have been made;[2,4] the complexities of the total kinetic situation (six norcaradiene–cycloheptatriene isomeric pairs and six dihydrobenzene derivatives all in equilibrium, linked by 36 rate constants) and the approximate kinetic analysis applied to the problem did not permit a thoroughly rigorous demonstration of kinetic control.[2,4] The stereochemical demonstration rests, then, on two sets of approximate rate constants or on the assumption that kinetic control prevails as (−)-**4** and (−)-**5** are formed from chiral **3** during the 381-min thermolysis at 180 °C. The rate constants $k(\mathbf{3} \rightarrow \mathbf{4}')$ and $k(\mathbf{3} \rightarrow \mathbf{5}')$ (cf. Scheme I, augmented by arrows for the direct interconversion of **4**′ and **5**′) must be approximately equal or the assignment of relative stereochemistry for **4** and **5** could be faulty and would in turn give an inaccurate assignment for **1** and **2**.

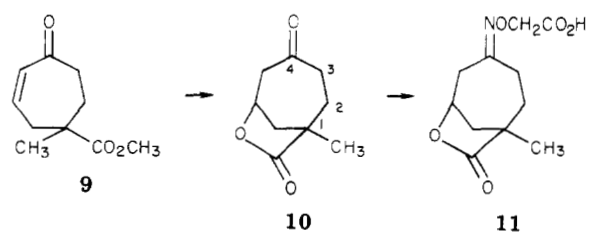
Results and Discussion

We sought an unambiguous determination of the relative stereochemistry of the chiral 2,7- and 3,7-dimethyl-7-(methoxymethyl)cycloheptatrienes through synthesis of a chiral precursor to both isomers, one possessing functionality suitable for selective introduction of methyl groups followed by conversion to the cycloheptatrienes. Consideration of these requirements led us to choose 5-(methoxycarbonyl)-5-methylcyclohept-2-en-1-one **9** as a key synthetic intermediate.

Synthesis of this cycloheptenone (Scheme II) began with the Diels–Alder reaction of 2-(trimethylsiloxy)buta-1,3-diene[5] and methyl methacrylate in refluxing xylenes to give the adduct **6** in 68% yield. The Simmons–Smith reaction of **6** with diiodomethane employing a zinc–silver couple[6] gave an 87% yield of the cyclopropanation product **7**. Treatment of this material with ferric chloride and pyridine in dimethylformamide gave a mixture of the β-chloro ketone **8** and the α,β-unsaturated ketone **9**.[7] This mixture was dehydrochlorinated with sodium acetate in refluxing methanol to yield the desired α,β-unsaturated ketone **9**.

Attempted hydrolysis of keto ester **9** under basic conditions gave no identifiable products. Hydrolysis of **9** with aqueous hydrochloric acid in 1,2-dimethoxyethane gave a 79% yield of 1-methyl-7-oxabicyclo[4.2.1]nonane-4,8-dione (**10**), an outcome corresponding to initial hydrolysis to the acid followed by Michael addition to the α,β-unsaturated ketone.

The literature reflects a dearth of convenient methods for resolution of ketones, yet one used previously with some cyclohexenone systems[8] proved quite satisfactory for our immediate needs. The *O*-(carboxymethyl)oxime **11** was

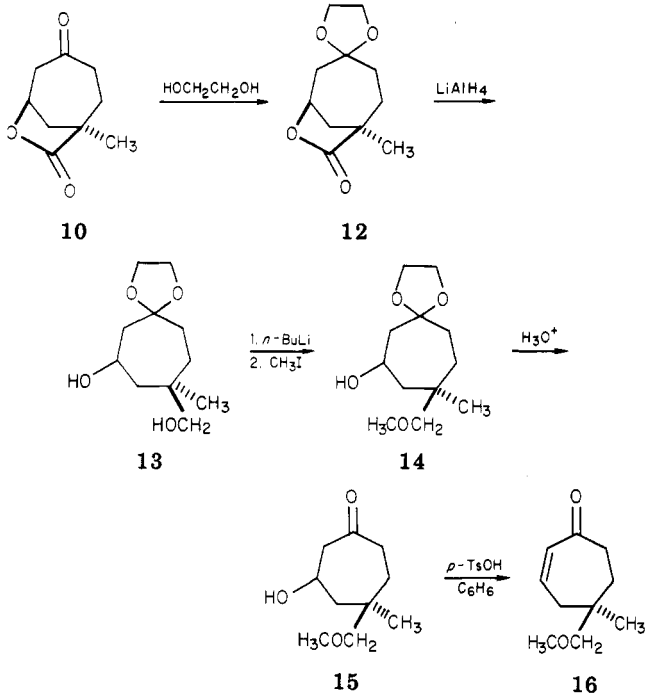


prepared in 84% yield by treatment of the keto lactone **10** with (carboxymethoxy)amine hemihydrochloride[9] in

(4) Klärner, F.-G. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 268–270.

(5) Jung, M. E.; McCombs, C. A. *Org. Synth.* **1978**, *58*, 163–167.
(6) Denis, J. M.; Girard, C.; Conia, J. M. *Synthesis* **1972**, 549–551.
(7) Ito, Y.; Fujii, S.; Saegusa, T. *J. Org. Chem.* **1976**, *41*, 2073–2074.
(8) Touboul, E.; Brienne, M.-J.; Jacques, J. *J. Chem. Res., Synop.* **1977**, 106; *J. Chem. Res., Miniprint* **1977**, 1182–1190.
(9) Anker, H. S.; Clarke, H. T. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. III, pp 172–174.

Scheme III



basic aqueous ethanol. The NMR spectrum and sharp melting point (113.5–115.0 °C) of this material were consistent with the formation of a single isomer, but no attempt was made to determine the stereochemistry of the oxime substituent.

Partial resolution of the *O*-(carboxymethyl)oxime **11** was accomplished by successive recrystallizations of its (−)-α-methylbenzylamine salt from 95% ethanol. The progress of the resolution was conveniently followed by NMR spectroscopy which showed two singlets for the diastereotopic C(1) methyl groups. The resolution gave two batches of salt, one of which was 17% diastereomerically pure enriched in the (+)-enantiomer of the keto lactone **10**; the other portion was 39% diastereomerically pure enriched in the (−) enantiomer.

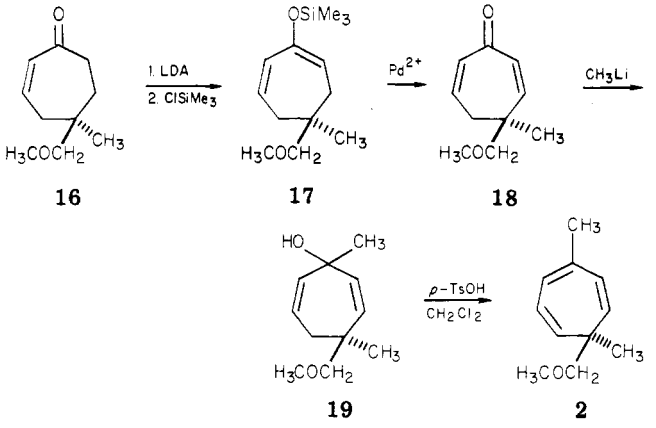
The portion of amine salt that was 17% diastereomerically pure was hydrolyzed with aqueous hydrochloric acid in 1,2-dimethoxyethane to give an 86% yield of the optically active keto lactone, $[\alpha]_D$ +8.6° ($CHCl_3$). This material was not recrystallized since it was found that the racemic modification crystallized preferentially from pentane–chloroform; concentration of the mother liquors gave material that was 77% optically pure as shown by NMR in the presence of an optically active shift reagent.

Having accomplished the desired resolution, we turned our efforts to the conversion of the chiral keto lactone **10** to an intermediate suitable for the introduction of the required methyl groups and elaboration to the cycloheptatrienes **1** and **2**. All further synthetic work was done by starting from 17% optically pure (+)-**10**.

Our immediate objective was 5-(methoxymethyl)-5-methylcyclohept-2-en-1-one, an intermediate which permitted selective introduction of methyl groups and which was anticipated to be less sensitive to the required synthetic manipulations than other plausible choices.

The synthesis of ether **16** outlined in Scheme III commenced with preparation of the ethylene ketal **12** by treatment of **10** with ethylene glycol and *p*-toluenesulfonic acid in refluxing benzene; the ketal **12** was obtained in 88% yield. It was reduced with lithium aluminum hydride in tetrahydrofuran to give the diol **13** in 96% yield. Attempts to hydrolyze the ketal at this stage led only to formation

Scheme IV



of a compound with an NMR spectrum consistent with 1-methyl-7-oxabicyclo[4.2.1]nonan-4-one, so a selective methylation of the diol at the hydroxymethyl function was sought. Treatment of the diol **13** with 1 equiv of *n*-butyllithium in tetrahydrofuran at 0 °C followed by iodomethane gave a mixture of the monomethyl ether **14** and unreacted diol **13**. The separation of **13** and **14** was very simple since the diol **13** was reasonably soluble in water; thus, concentration of the reaction mixture followed by treatment with chloroform and extraction with water gave very clean monomethyl ether. The unreacted diol **13** could then be obtained by saturating the aqueous solution with salt followed by repeated chloroform extractions. The recovered diol **13** was methylated again as described above to give the monomethyl ether **14** in a total yield of 87%.

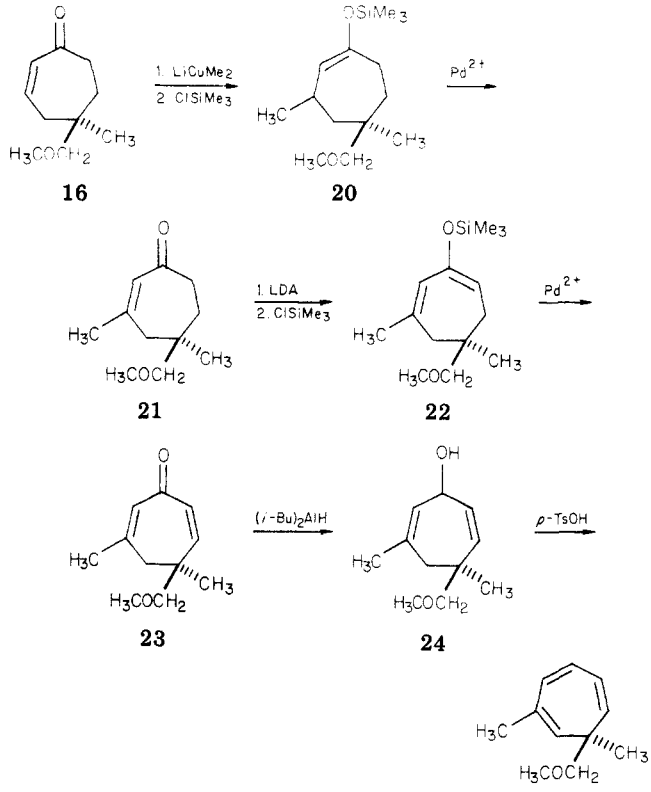
The monomethyl ether **14** was hydrolyzed with aqueous hydrochloric acid in 1,2-dimethoxyethane to yield a mixture of the β-hydroxy ketone **15** and the α,β-unsaturated ketone **16**. This mixture was dehydrated with *p*-toluenesulfonic acid in refluxing benzene to provide the α,β-unsaturated ketone **16** in 54% yield after column chromatography.

The conversion of **16** to 3,7-dimethyl-7-(methoxymethyl)cycloheptatriene (**2**) was accomplished as outlined in Scheme IV. Formation of the kinetic enolate of **16** with lithium diisopropylamide in tetrahydrofuran at −78 °C followed by trapping of the enolate with chlorotrimethylsilane gave the silyl enol ether **17**; this material was oxidized to the di-α,β-unsaturated ketone **18** withour purification.

There are a number of methods in the literature for oxidizing silyl enol ethers to the corresponding α,β-unsaturated ketones;[10–13] we elected to use the procedure provided by Saegusa and co-workers[13] which involves treatment of the ether with palladium(II) acetate, employing acetonitrile as the solvent. This reaction can be carried out by using a stoichiometric amount of $Pd(OAc)_2$ or 0.5 equiv of $Pd(OAc)_2$ and 0.5 equiv of *p*-benzoquinone which apparently functions to regenerate the active palladium(II) species. The method using a stoichiometric amount of palladium(II) acetate avoids the separation of hydroquinone from the product and was the procedure employed. Treatment of **17** with 1 equiv of $Pd(OAc)_2$ in acetonitrile at room temperature gave the di-α,β-unsaturated ketone **18** in 54% yield from the α,β-unsaturated ketone **16**.

(10) Jung, M. E.; Pan, Y.-G.; Rathke, M. W.; Sullivan, D. F.; Woodbury, R. P. *J. Org. Chem.* **1977**, *42*, 3961–3963.
(11) Ryu, I.; Murai, S.; Hatayama, Y.; Sonoda, N. *Tetrahedron Lett.* **1978**, 3455–3458.
(12) Fleming, I.; Paterson, I. *Synthesis* **1979**, 736–738.
(13) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011–1013.

Scheme V

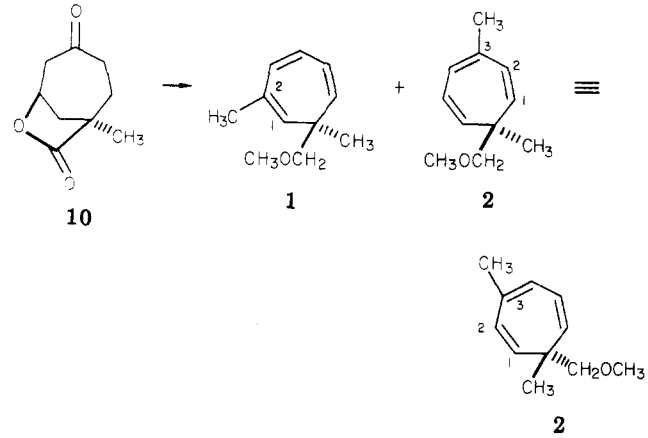


The ketone **18** was methylated with methyllithium in ether to yield a mixture of the alcohol **19** and the cycloheptatriene **2**. This mixture was treated with *p*-toluenesulfonic acid in refluxing dichloromethane to give triene **2** in 70% yield for the two steps. The ^1H NMR spectrum and chromatographic behavior of this material were identical with those of a sample of (±)-**2** prepared by an alternative synthetic route.[3] The chiral sample of **2** prepared through the steps in Scheme IV exhibited a specific rotation of $[\alpha]_{436}$ −5.6° ($CHCl_3$). The NMR spectrum of this material in benzene-d_6 in the presence of the chiral shift reagent Eu(hfbc)$_3$ showed it to be 17.6 ± 1.6% optically pure.

The preparation of the 2-methyl isomer from the ketone **16** outlined in Scheme V involved chemistry very similar to that used to prepare the 3-methyl compound. Treatment of **16** with lithium dimethylcuprate in ether followed by chlorotrimethylsilane gave the enol ether **20** which was oxidized to the α,β-unsaturated ketone **21** without purification. The ketone **21** was converted to the di-α,β-unsaturated ketone **23** by the previously described methods.

The reduction of **23** to the alcohol **24** was initially attempted with sodium borohydride, but this reagent led to formation of a substantial amount of the 1,4-addition product. This complication was overcome by the use of diisobutylaluminum hydride which gave the alcohol **24** and very little, if any, of the 1,4-addition product. The alcohol **24** was dehydrated without purification by treatment with *p*-toluenesulfonic acid in refluxing dichloromethane to give 2,7-dimethyl-7-(methoxymethyl)cycloheptatriene (**1**). Spectral data for this material were consistent with the assigned structure and are comparable to the spectral data reported by Brassel.[14] The NMR spectrum in the presence of the optically active shift reagent Eu(hfbc)$_3$ showed this material to be 16.2 ± 1.8% optically pure; it had a rotation of $[\alpha]_{436}$ −7.7° ($CHCl_3$).

Scheme VI



These syntheses of chiral **1** and **2** from the common chiral precursor keto lactone (+)-**10** are summarized stereochemically in Scheme VI: they demonstrate that when these isomers have the same relative stereochemistry at C(7), they have opposite signs of rotation.

The stereochemical conclusion reached in this work thus confirms the assignment of relative stereochemistry made by Klärner and Brassel[1] and confirms as well that the thermal rearrangement of **1** to **2** with a change in the sign of rotation proceeds largely with inversion of configuration at the chiral center (**1** ⇄ **1′** ⇄ **2′** ⇄ **2**).

Experimental Section

Elemental analyses and electron-impact mass spectra were determined by Dr. Richard A. Wielesek using CEC-21-110B or Hewlett-Packard 5930A instruments.

Routine proton NMR spectra were obtained on a Varian-XL-100-15A instrument operating at 100 MHz by employing deuteriochloroform as the solvent unless otherwise stated. Chemical shifts are given in parts per million (ppm) and are referenced either to tetramethylsilane (δ 0.00) or the residual proton signal in the deuteriochloroform (δ 7.27); coupling constants are given in hertz. Carbon-13 NMR spectra were determined on the same instrument operating at 25.2 MHz and are also referenced to internal tetramethylsilane. Preparative and analytical vapor-phase chromatography (VPC) was carried out on a Varien 1520 instrument employing a thermal-conductivity detector. The FFAP column was 6.4 mm × 2 m of 10% FFAP on 60/80 Chromosorb W NAW. Infrared spectra were determined on a Beckmann IR-7 instrument. Melting points were determined on a Koefler hot-stage apparatus and are uncorrected. Boiling points given for Kugelrohr distillations are the oven air temperature ranges over which the compounds were collected and do not represent true boiling points. The reaction temperatures specified are the temperatures of the heating or cooling baths and do not necessarily represent the temperatures of reaction mixtures. Unless otherwise stated, "concentrated" implies concentration using a rotary evaporator at a pressure of approximately 25 mm.

All solvents used in this study were reagent grade or distilled prior to use. Solvents were dried by distillation under a dry nitrogen atmosphere as follows: ether was distilled from lithium aluminum hydride, tetrahydrofuran (THF) was distilled from a deep purple solution of the sodium benzophenone ketyl, acetonitrile was distilled from calcium hydride, and amines were distilled from potassium hydroxide.

2-(Trimethylsiloxy)buta-1,3-diene was prepared in 46% yield by the method of Jung and McCombs[6] from 3-buten-2-one (0.36 mol) and chlorotrimethylsilane (0.40 mol). Fractional distillation through a 25-cm glass-helix-packed column afforded diene of boiling point 40–44 °C (50 mm) [lit.[5] bp 50–55 °C (50 mm)].

4-Methyl-4-(methoxycarbonyl)-1-(trimethylsiloxy)cyclohex-1-ene (6). A solution of 2-(trimethylsiloxy)buta-1,3-diene (37.5 g, 0.264 mol), methyl methacrylate (135 g, 1.35 mol), and 4,4′-methylenebis(2,6-di-*tert*-butylphenol) (1.0 g) in xylenes (300 mL) was heated at reflux under a nitrogen atmosphere for 48 h.

(14) Brassel, B. Diplomarbeit, University of Bochum, 1979.

The reaction mixture was concentrated at reduced pressure (45 mm), and the residue was fractionally distilled through a 5-cm vacuum-jacketed Vigreux column to give 43.4 g (67.9%) of the adduct as a clear colorless liquid, bp 60–64 °C (0.05 mm). The analytical sample was purified by VPC on a 6.4 mm × 1.2 m 20% SE-30 on 60/80 Chromosorb W column at 150 °C: NMR δ 0.18 (9 H, s), 1.20 (3 H, s), 1.52–2.72 (6 H, m), 3.86 (3 H, s), 4.80 (1 H, m); IR (neat): 2965, 1735, 1670, 1250, 1180, 880, 835 cm^{-1}; mass spectrum, m/z (relative intensity) 242 (m^+, 19), 183 (100), 125 (52), 75 (48), 73 (52).

Anal. Calcd for $C_{12}H_{22}O_3Si$: C, 59.46; H, 8.86. Found: C, 59.80; H, 9.15.

4-Methyl-4-(methoxycarbonyl)-1-(trimethylsiloxy)bicyclo[4.1.0]heptane (7). A hot solution of silver acetate (0.71 g, 4.3 mmol) in glacial acetic acid (250 mL) was stirred under nitrogen and 20 mesh granular zinc (43.0 g, 0.658 mol) was added in one portion; the resulting mixture was stirred for 5 min. The acetic acid was decanted, the Ag–Zn couple was washed with ether (5 × 150 mL) and covered with ether (500 mL), and a spatula tip full of powdered silver metal was added. Diiodomethane (27.0 mL, 89.8 g, 0.335 mol) was added dropwise over a 15-min period, and the resulting mixture was stirred at room temperature for 1 h. 4-Methyl-4-(methoxycarbonyl)-1-(trimethylsiloxy)cyclohex-1-ene (46.9 g, 0.194 mol) was added dropwise over a 10-min period, and the reaction mixture was heated at reflux for 22 h. The reaction mixture was cooled (0 °C), and pyridine (71 mL) was added dropwise over a 45-min period; this mixture was warmed to room temperature and stirred for 30 min. The zinc salts were removed by filtration and washed well with ether; the combined filtrate and washes were concentrated to give an orange oil. This material was Kugelrohr distilled (70–90 °C, 0.1 mm) to yield 43.2 g (87.1%) of a clear, colorless liquid. The analytical sample was purified by VPC (6.4 mm × 1.2 m 20% SE-30 on 60/80 Chromosorb W column, 150 °C): NMR δ 0.00–0.30 (11 H, m), 0.62–1.40 (6 H, m), 1.52–2.26 (3 H, m), 2.55–2.94 (1 H, m), 3.70 (3 H, s); IR (neat) 2940, 1730, 1465, 1368, 1250, 1210, 1165, 1125, 1078, 865, 840 cm^{-1}; mass spectrum, m/z (relative intensity) 256 (m^+, 45), 197 (53), 141 (83), 75 (100), 73 (67); exact mass calcd for $C_{13}H_{24}O_3Si$ m/z 256.149, found 256.149.

5-Methyl-5-(methoxycarbonyl)cyclohept-2-en-1-one (9). A solution of ferric chloride hexahydrate (167 g, 0.62 mol) in dimethylformamide (DMF; 400 mL) was cooled (0 °C) under a nitrogen atmosphere, and a solution of 4-methyl-4-(methoxycarbonyl)-1-(trimethylsiloxy)bicyclo[4.1.0]heptane (40.2 g, 0.155 mol) and pyridine (15.0 g, 0.19 mol) in DMF (500 mL) was added over a 1.5-h period. The cooling bath was removed, and the reaction mixture was stirred for an additional 3 h. The reaction mixture was poured into ice-cold 10% aqueous HCl (2 L) and extracted with ether (5 × 400 mL). The combined ether extracts were washed (10% HCl, 3 × 300 mL), dried ($MgSO_4$), filtered, and concentrated to give 31.6 g of an orange oil. Analysis by NMR showed this material to be a mixture of the β-chloro ketone **8** and the α,β-unsaturated ketone **9**. This oil and sodium acetate (32.0 g, 0.39 mol) were dissolved in methanol (500 mL), and the resulting solution was heated at reflux under a nitrogen atmosphere for 3 h. The reaction mixture was concentrated, and the residue was treated with water (200 mL) and extracted with ether (3 × 150 mL). The combined ether extracts were washed (water, brine), dried ($MgSO_4$), filtered, and concentrated to leave an orange oil. Kugelrohr distillation [70–90 °C (0.05 mm)] gave 21.9 g of crude α,β-unsaturated ketone as a light yellow liquid. Analysis by VPC on the FFAP column at 165 °C showed this material to contain 68% of the desired α,β-unsaturated ketone. The analytical sample collected by VPC on the FFAP column was characterized: NMR δ 1.30 (3 H, s), 1.62–1.92 (1 H, m), 2.05–2.67 (4 H, m), 2.70–2.95 (1 H, m), 3.70 (3 H, s), 6.03 (1 H, d, J = 12), 6.57 (1 H, dt, J_d = 10, J_t = 6); IR (neat) 2940, 1735, 1670, 1460, 1390, 1200, 1160, 1110 cm^{-1}; mass spectrum, m/z (relative intensity): 182 (m^+, 28), 123 (100), 95 (94), 79 (61).

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.92; H, 7.74. Found: C, 65.84; H, 8.08.

1-Methyl-7-oxabicyclo[4.2.1]nonane-4,8-dione (10). A solution of crude 5-methyl-5-(methoxycarbonyl)cyclohept-2-en-1-one (49.0 g, 0.18 mol) in 1,2-dimethoxyethane (250 mL) was treated with 18% aqueous HCl (80 mL), and the resulting solution was stirred at 50 °C under a nitrogen atmosphere for 14 h. The dark orange mixture was poured into brine (500 mL) and extracted with chloroform (4 × 100 mL). The combined chloroform extracts were washed (brine), dried ($MgSO_4$), filtered, and concentrated to yield an oily orange solid. This material was Kugelrohr distilled [80–120 °C (0.1 mm)] to give 37.6 g of an oily white solid. This solid was recrystallized from chloroform–hexanes; 24.0 g (79.4%) of the keto lactone was obtained as a white crystalline solid: mp 94–96 °C; ^1H NMR δ 1.34 (3 H, s), 1.46–2.10 (3 H, m), 2.34–3.14 (5 H, m), 4.75–4.94 (1 H, m); ^1H decoupled ^{13}C NMR ($CDCl_3$) 23.6, 34.5, 40.1, 40.8, 43.2, 50.0, 71.7, 179.8, 208.1; IR ($CDCl_3$) 2980, 1775, 1715, 1345, 1195, 1085 cm^{-1}; mass spectrum, m/z (relative intensity) 168 (m^+, 98), 140 (20), 95 (71), 82 (100), 81 (77), 69 (62).

Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.20; H, 6.99.

4-[(Carboxymethoxy)imino]-1-methyl-8-oxo-7-oxabicyclo[4.2.1]nonane (11). A solution of 1-methyl-7-oxabicyclo[4.2.1]nonane-4,8-dione (24.2 g, 0.144 mol) and (carboxymethoxy)amine hemihydrochloride (16.0 g, 0.0734 mol) in 95% ethanol (450 mL) was made basic (pH 10) with 10% aqueous sodium hydroxide, and the resulting solution was heated at reflux for 4 h. The reaction mixture was concentrated to a volume of approximately 250 mL and poured into water (100 mL). The resulting solution was washed with chloroform (1 × 100 mL), acidified to pH 1 with concentrated HCl, and extracted with chloroform (5 × 75 mL). The combined chloroform extracts were washed (brine), dried ($MgSO_4$), filtered, and concentrated to give a clear colorless oil. This material was crystallized from chloroform–hexanes; 29.0 g (83.6%) of the carboxymethoxime was obtained as a white solid: mp 113.5–115 °C; NMR δ 1.30 (3 H, s), 1.52–2.98 (7 H, m), 3.15–3.60 (1 H, m), 4.65 (2 H, s), 3.72–3.92 (1 H, m), 9.62 (1 H, s); IR ($CHCl_3$) 3600–2960, 1765, 1745, 1455, 1250, 1100, 1025, 890 cm^{-1}; mass spectrum, m/z (relative intensity) 241 (m^+, 0.1), 167 (42), 108 (29), 81 (100); exact mass calcd for $C_{11}H_{15}NO_5$ m/z 241.095, found 241.095.

Preparation and Resolution of the (−)-α-Methylbenzylamine Salt of 4-[(Carboxymethoxy)imino]-1-methyl-8-oxo-7-oxabicyclo[4.2.1]nonane. A solution of 4-[(carboxymethoxy)imino]-1-methyl-8-oxo-7-oxabicyclo[4.2.1]nonane (29.0 g, 0.120 mol) in chloroform (250 mL) was treated with (−)-α-methylbenzylamine (15.0 g, 0.120 mol, Aldrich), and the resulting solution was stirred at room temperature for 15 min. The solvent was removed by rotary evaporation, and the white solid residue was washed well with ether and dried to give 43.0 g (98.6%) of the amine salt: NMR δ 1.27 and 1.29 (3 H, 2 s for diastereotopic C(1) methyl groups), 1.53 (3 H, d, J = 6), 1.6–2.8 (7 H, m), 3.0–3.5 (1 H, m), 4.04–4.36 (3 H, m), 4.6–4.78 (1 H, m), 7.35 (5 H, s), 8.00 (3 H, s); IR (KBr) 3060, 3020, 1760, 1580, 1405, 1320, 1205, 1075 cm^{-1}.

The amine salt was resolved through successive recrystallizations from 95% ethanol. In a typical recrystallization, the amine salt was dissolved in the minimum amount of hot 95% ethanol (about 9 mL/g of salt), and the solution was allowed to stand at room temperature overnight. The crystals formed were filtered, and the mother liquors were cooled in a freezer to approximately −28 °C to yield a second crop of crystals. A third crop could be obtained by the addition of ether followed by cooling in a freezer.

The progress of the resolution was conveniently followed by ^1H NMR observation of the relative ratios of the diastereotopic C(1) methyl signals. The C(1) methyl signal at δ 1.29 corresponded to the (+) enantiomer of the keto lactone **10**, and the signal at δ 1.27 corresponded to the (−) enantiomer. Five recrystallizations from 95% ethanol gave 15.4 g of material with a diastereomeric purity of 39%, enriched in the (−) enantiomer of keto lactone **10**. A second batch of material (19.8 g) was obtained from second and third crops and was 17% diastereomerically pure, enriched in the (+) enantiomer of keto lactone **10**.

Hydrolysis of the Amine Salt of 11. A solution of the amine salt (19.8 g, 0.055 mol, 17% diastereomerically pure) in 1,2-dimethoxyethane (300 mL) was treated with water (100 mL) and concentrated hydrochloric acid (200 mL). The resulting solution was stirred at reflux for 85 h, cooled, poured into brine (700 mL), and extracted with chloroform (4 × 200 mL). The combined chloroform extracts were washed (saturated $NaHCO_3$, brine), dried ($MgSO_4$), filtered, and concentrated to yield 7.95 g (86.5%) of keto lactone **10** as a light yellow solid. This material had $[\alpha]_D$ +8.6° ($CHCl_3$); ^1H NMR in the presence of Eu(hfbc)$_3$ in C_6D_6 showed

this material to be 17% optically pure. The ^1H NMR spectrum of the keto lactone in $CDCl_3$ was identical with that of a previously prepared racemic sample.

4,4-(Ethylenedioxy)-1-methyl-7-oxabicyclo[4.2.1]nonan-8-one (12). A solution of ethylene glycol (125 g, 2.0 mol) and *p*-toluenesulfonic acid monohydrate (0.5 g) in benzene (500 mL) was heated at reflux under a nitrogen atmosphere in a flask fitted with a Dean–Stark trap until the water level in the trap was constant. The water was drained from the trap, and a solution of 1-methyl-7-oxabicyclo[4.2.1]nonane-4,8-dione (7.44 g, 0.0443 mol) in benzene (50 mL) was added to the reaction flask; this mixture was heated at reflux for 7 h. The reaction mixture was washed (10% NaOH, H_2O, brine), dried (K_2CO_3), filtered, and concentrated to yield 8.27 g (88.2%) of the ketal as a light yellow solid. Recrystallization from pentane–chloroform provided the analytical sample as a white crystalline solid: mp 75–76 °C; NMR δ 1.28 (3 H, s), 1.58–2.68 (8 H, m), 3.80–4.10 (4 H, m), 4.60–4.82 (1 H, m); IR ($CHCl_3$) 3000, 2960, 2840, 1765, 1458, 1385, 1348, 1165, 1110 cm^{-1}; mass spectrum, *m/z* (relative intensity) 212 (m^+, 18), 184 (15), 139 (18), 115 (11), 99 (80), 86 (100).

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.24; H, 7.60. Found: C, 62.25; H, 7.95.

1,1-(Ethylenedioxy)-3-hydroxy-5-(hydroxymethyl)-5-methylcycloheptane (13). A solution of 4,4-(ethylenedioxy)-1-methyl-7-oxabicyclo[4.2.1]nonan-8-one (8.2 g, 0.039 mol) in dry THF (400 mL) was cooled (0 °C) under a nitrogen atmosphere, and lithium aluminum hydride (2.0 g, 0.053 mol) was added portionwise over a 5-min period. The resulting mixture was stirred at 0 °C for 30 min, warmed to room temperature, and stirred for 21 h. The reaction mixture was cooled (0 °C) and treated successively with water (2 mL), 15% NaOH (2 mL), and water (6 mL). The resulting mixture was dried (Na_2SO_4) and filtered; the solids collected were washed well with chloroform. The combined filtrate and washes were concentrated, and the residue was dried in an Abderhalden pistol (56 °C, 0.05 mm) for 24 h to yield 8.1 g (96.4%) of the diol as a white crystalline solid. The analytical sample was recrystallized from pentane–chloroform: mp 89–90 °C; NMR δ 0.95 (3 H, s), 1.20–2.10 (8 H, m), 2.44 (2 H, s), 3.33 (2 H, s), 3.86–4.20 (5 H, m); IR ($CHCl_3$) 3400, 3000, 2940, 2860, 1105, 1095, 1030 cm^{-1}; mass spectrum, *m/z* (relative intensity) 216 (m^+, <0.01), 140 (0.11), 114 (100), 98 (41).

Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 61.28; H, 9.18.

1,1-(Ethylenedioxy)-3-hydroxy-5-(methoxymethyl)-5-methylcycloheptane (14). A solution of 1,1-(ethylenedioxy)-3-hydroxy-5-(hydroxymethyl)-5-methylcycloheptane (7.70 g, 0.0356 mol) in dry THF (225 mL) was cooled (0 °C) under a nitrogen atmosphere, and a 1.2 M hexane solution of *n*-butyllithium (38.5 mL, 0.046 mol) was added dropwise over a 15-min period. The resulting solution was stirred at 0 °C for 10 min at which time iodomethane (5.7 mL, 13.0 g, 0.0916 mol) was added; this solution was stirred at 0 °C for 15 min, warmed to room temperature, and stirred for 3 h. The reaction mixture was concentrated, and the residue was dissolved in chloroform (300 mL). The chloroform solution was washed (H_2O, brine), dried (K_2CO_3), filtered, and concentrated to give 5.80 g of the monomethyl ether **14** as a yellow oil.

The aqueous washes from above were saturated with sodium chloride and extracted with chloroform (8 × 100 mL); the combined chloroform extracts were dried (K_2CO_3), filtered, and concentrated to yield 1.90 g of unreacted diol **13**. This material was dissolved in dry THF (20 mL) and cooled (0 °C) under a nitrogen atmosphere, and a 1.2 M hexane solution of *n*-butyllithium (9.5 mL, 0.01 mol) was added dropwise over a 15-min period. The reaction mixture was stirred at 0 °C for 15 min at which time iodomethane (1.4 mL, 3.2 g, 0.023 mol) was added, and this solution was warmed to room temperature and stirred for 3 h. A workup as described above gave 1.30 g of the monomethyl ether **14** as a yellow oil. A total of 7.10 g (86.6%) of the monomethyl ether **14** was obtained. The analytical sample was purified by VPC on a 6.4 mm × 1 m 10% SE-30 on 60/80 Chromosorb W column at 160 °C: NMR δ 0.98 (3 H, s), 1.26–2.22 (9 H, m), 3.05 (2 H, s), 3.33 (3 H, s), 3.80–4.26 (5 H, m); IR (neat) 3400, 2920, 2850, 1465, 1455, 1375, 1360, 1110, 1035 cm^{-1}; mass spectrum, *m/z* (relative intensity) 230 (m^+, <0.01), 115 (100), 99 (75); exact mass calcd for $C_{12}H_{22}O_4$ *m/z* 230.152, found 230.152.

5-(Methoxymethyl)-5-methylcyclohept-2-en-1-one (16). A solution of 1,1-(ethylenedioxy)-3-hydroxy-5-(methoxymethyl)-cycloheptane (6.9 g, 0.03 mol) in 1,2-dimethoxyethane (200 mL) was treated with 10% HCl (100 mL), and the resulting solution was stirred at room temperature for 23 h. The reaction mixture was concentrated to a volume of approximately 150 mL on a rotary evaporator, and the concentrate was poured into brine (100 mL). The resulting mixture was extracted with ether (3 × 150 mL), and the combined ether extracts were washed (H_2O, 5% $NaHCO_3$, brine), dried ($MgSO_4$), filtered, and concentrated to yield 4.2 g of a yellow liquid. This material consisted of a mixture of 3-hydroxy-5-(methoxymethyl)-5-methylcycloheptan-1-one (**15**) and the desired α,β-unsaturated ketone **16**. The aqueous layers from the above workup were saturated with NaCl and extracted with chloroform (3 × 75 mL). The chloroform extracts were dried ($MgSO_4$), filtered, and concentrated to yield 1.6 g of a mixture of **15** and **16** as a yellow liquid.

The two mixtures of **15** and **16** were combined and dissolved in benzene (100 mL), and catalytic amount of *p*-toluenesulfonic acid monohydrate was added. The resulting solution was heated at reflux for 2 h under nitrogen in a flask fitted with a Dean–Stark trap. The reaction mixture was washed (saturated $NaHCO_3$, brine), dried ($MgSO_4$), filtered, and concentrated to yield 3.56 g of the crude α,β-unsaturated ketone **16** as a yellow liquid. This material was purified by column chromatography on 200 g of silica gel with chloroform as the eluent to give a series of 50-mL fractions; fractions 10–20 contained 2.72 g (54%) of the α,β-unsaturated ketone **16** as a light yellow liquid. The analytical sample was purified on the FFAP column at 150 °C: NMR δ 1.00 (3 H, s), 1.25–1.94 (2 H, m), 2.04–2.70 (4 H, m), 3.15 (2 H, s), 3.36 (3 H, s), 6.04 (1 H, d, J = 12), 6.44–6.76 (1 H, m); IR 2880, 2840, 1660, 1380, 1100, 800 cm^{-1}; mass spectrum, *m/z* (relative intensity): 168 (m^+, 30), 123 (100), 95 (38), 93 (55), 79 (39).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.73; H, 9.21.

4-Methyl-4-(methoxymethyl)cyclohepta-2,6-dien-1-one (18). A solution of diisopropylamine (3.6 mL, 2.5 g, 0.025 mol) in dry THF (25 mL) was cooled (0 °C) under a nitrogen atmosphere, and a 1.0 M hexane solution of *n*-butyllithium (13 mL, 0.013 mol) was added. The resulting solution was stirred at 0 °C for 10 min and cooled to −78 °C, and a solution of 5-methyl-5-(methoxymethyl)cyclohept-2-en-1-one [1.20 g, 7.14 mmol; derived from 17% optically pure (+) keto lactone **10**] in dry THF (8 mL) was added dropwise over a 15-min period. The reaction mixture was stirred at −78 °C for 15 min at which time triethylamine (5.0 mL, 3.6 g, 0.036 mol) and chlorotrimethylsilane (4.5 mL, 3.9 g, 0.036 mol) were added; this solution was stirred at −78 °C for 15 min, warmed to room temperature, and stirred for an additional 15 min. The resulting mixture was poured into a mixture of ether (50 mL) and water (50 mL), and the organic layer was separated, washed (H_2O, saturated $NaHCO_3$), dried (K_2CO_3), filtered, and concentrated to yield 2.2 g of an orange liquid. This liquid was dissolved in dry acetonitrile (10 mL), deoxygenated with a stream of nitrogen (20 min), and added to a similarly deoxygenated solution of palladium(II) acetate (2.0 g, 8.9 mmol) in dry acetonitrile (50 mL); the resulting mixture was stirred under a nitrogen atmosphere at room temperature for 18 h. The reaction mixture was filtered through a pad of silica gel, and the silica gel was rinsed well with ether. The combined filtrate and rinses were washed (10% HCl, H_2O, saturated $NaHCO_3$, brine), dried ($MgSO_4$), filtered, and concentrated to yield 0.89 g of a brown liquid. This material was Kugelrohr distilled [65–75 °C (0.05 mm)] to give 0.64 g (54%) of the dienone **18** as a light yellow liquid. The analytical sample was purified by VPC on the FFAP column at 170 °C: NMR δ 1.16 (3 H, s), AB portion of an ABX pattern centered at 2.52 (2 H, $\Delta\nu$ = 38 Hz, J_{AB} = 17, J_{AX} = J_{BX} = 5, further split by a long-range coupling, J = 1), 3.24 (2 H, AB, $\Delta\nu$ = 18 Hz, J = 8), 3.35 (3 H, s), 5.90–6.60 (4 H, m); IR ($CDCl_3$) 2960, 2910, 2850, 2810, 1648, 1605, 1405, 1110, 855 cm^{-1}; mass spectrum, *m/z* (relative intensity) 166 (m^+, 45), 121 (100), 91 (45), 77 (35).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.10; H, 8.57.

(−)-3,7-Dimethyl-7-(methoxymethyl)cyclohepta-1,3,5-triene ((−)-2). A solution of 4-methyl-4-(methoxymethyl)cyclohepta-2,6-dien-1-one (0.47 g, 2.8 mmol) in dry ether (60 mL) was cooled (0 °C) under a nitrogen atmosphere, and a 1.3 M ether solution

of methyllithium (3.8 mL, 4.9 mmol) was added; the resulting solution was stirred at 0 °C for 15 min, warmed to room temperature, and stirred for an additional 15 min. The reaction mixture was poured into ice-cold 10% HCl (30 mL) and extracted with ether (3 × 20 mL); the combined ether extracts were washed (H_2O, brine), dried ($MgSO_4$), filtered, and concentrated to yield 0.48 g of a yellow liquid. Analysis by NMR showed this material to be a mixture of the alcohol **19** and the triene **2**. This liquid and a catalytic amount of *p*-toluenesulfonic acid monohydrate were dissolved in dichloromethane (25 mL) and heated at reflux under a nitrogen atmosphere for 2 h. The reaction mixture was concentrated, and the residue was dissolved in ether (30 mL). The ether solution was washed (saturated $NaHCO_3$, brine), dried ($MgSO_4$), filtered, and concentrated to give 0.37 g of an orange liquid. Column chromatography on silica gel (20 g) with chloroform as the eluent gave 0.32 g (69.6%) of triene **2** as a yellow liquid. The ^1H NMR spectrum of this material was identical with the spectrum of 3,7-dimethyl-7-(methoxymethyl)cyclohepta-1,3,5-triene prepared by an alternative synthetic route.[3] A sample purified by VPC on the FFAP column at 120 °C had $[\alpha]_{436}$ −5.60 ± 0.15° (*c* 0.0296 g/mL, $CHCl_3$).

The optical purity of this material was determined by NMR by employing tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III) and benzene-d_6 as the solvent. The shift reagent was added portionwise until the C(7) methyl resonance was cleanly split into two singlets at 2.93 and 3.02 ppm. The average of 13 integrations showed this material to be 17.6 ± 1.6% optically pure. The C(7) methyl resonance at 2.93 corresponded to the (−) enantiomer.

3,5-Dimethyl-5-(methoxymethyl)cyclohept-2-en-1-one (21). A slurry of cuprous iodide (3.2 g, 0.0168 mol) in dry ether (125 mL) was cooled (0 °C) under a nitrogen atmosphere, and a 1.3 M ethereal solution of methyllithium (26 mL, 0.034 mol) was added. Additional cuprous iodide was added in small portions until a faint yellow color persisted, and the resulting mixture was stirred at 0 °C for 10 min. A solution of 5-methyl-5-(methoxymethyl)cyclohept-2-en-1-one [1.40 g, 8.33 mmol; derived from 17% optically pure (+) keto lactone **10**] in dry ether (10 mL) was added dropwise over a 15-min period, and the resulting mixture was stirred at 0 °C for 3 h. Triethylamine (13.0 mL, 9.4 g, 0.093 mol) and chlorotrimethylsilane (9.5 mL, 8.1 g, 0.075 mol) were added, and the resulting mixture was stirred at 0 °C for 1 h. The reaction mixture was poured into pentane (125 mL), washed (saturated $NaHCO_3$, brine), dried (Na_2SO_4), filtered, and concentrated to yield 1.84 g of the crude silyl enol ether as a yellow liquid. This liquid was dissolved in dry acetonitrile (20 mL), deoxygenated with a stream of nitrogen (15 min), and added to a similarly deoxygenated solution of palladium(II) acetate (1.60 g, 7.1 mmol) in acetonitrile (40 mL). The reaction mixture was stirred at room temperature for 22 h, and then the solids were removed by filtration through a pad of silica gel and rinsed well with ether. The combined filtrate and rinses were washed (10% HCl, saturated $NaHCO_3$, brine), dried ($MgSO_4$), filtered, and concentrated to yield 1.15 g of an orange liquid. This material was Kugelrohr distilled [70–75 °C (0.25 mm)] to give 1.00 g of the enone as a light yellow liquid. Analysis by VPC on the FFAP column at 170 °C showed this material to contain 61% of the desired enone. The analytical sample collected on the FFAP column was characterized: NMR δ 1.00 (3 H, s), 1.32–1.80 (2 H, m), 1.98 (3 H, s), 2.08–2.58 (4 H, m), 3.10 (2 H, s), 3.34 (3 H, s), 5.92 (1 H, s); IR ($CDCl_3$) 2940, 2900, 2840, 1645, 1105 cm^{-1}; mass spectrum, *m/z* (relative intensity) 182 (m^+, 55), 137 (100), 95 (80), 85 (78).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.61; H, 9.75.

3,5-Dimethyl-5-(methoxymethyl)cyclohepta-2,6-dien-1-one (23). A solution of diisopropylamine (2.7 mL, 2.0 g, 0.019 mol) in dry THF (25 mL) was treated with a 1.0 M hexane solution of *n*-butyllithium (10 mL, 0.010 mol), and the resulting solution was stirred at room temperature under a nitrogen atmosphere for 5 min. The reaction mixture was cooled (−78 °C), and a solution of crude 3,5-dimethyl-5-(methoxymethyl)cyclohept-2-en-1-one (0.94 g, 61% pure, 3.2 mmol) in dry THF (5 mL) was added dropwise over a 20-min period. The resulting solution was stirred at −78 °C for 20 min at which time chlorotrimethylsilane (3.5 mL, 3.0 g, 0.028 mol) and triethylamine (4.0 mL, 2.9 g, 0.029 mol) were added; this solution was stirred at −78 °C for 10 min, warmed to room temperature, and stirred for 1 h. The reaction mixture was poured into ether (75 mL), washed (H_2O, saturated $NaHCO_3$), dried (K_2CO_3), filtered, and concentrated to yield 2.01 g of a yellow liquid. This liquid was dissolved in dry acetonitrile (10 mL), deoxygenated with a stream of nitrogen (15 min), and added to a deoxygenated solution of palladium(II) acetate (1.3 g, 5.8 mmol) in dry acetonitrile (50 mL). The reaction mixture was stirred under a nitrogen atmosphere for 22 h, and then the solids were removed by filtration through a pad of silica gel and rinsed well with ether. The combined filtrate and rinses were washed (10% HCl, H_2O, saturated $NaHCO_3$), dried ($MgSO_4$), filtered, and concentrated to give 1.18 g of an orange liquid. This material was Kugelrohr distilled [65–75 °C (0.05 mm)] to yield 0.99 g of the dienone **23** as a yellow liquid. Analysis by VPC on the FFAP column showed this material to contain 59% of the dienone **23**. The analytical sample was purified by VPC on the FFAP column at 165 °C: NMR δ 1.16 (3 H, s), 2.00 (3 H, s), 2.50 (2 H, AB, $\Delta\nu$ = 43 Hz, J = 16, further split by a long range coupling, J = 1), 3.25 (2 H, AB, $\Delta\nu$ = 18 Hz, J = 8), 3.37 (3 H, s), 5.88–6.42 (3 H, m); IR ($CDCl_3$) 2940, 2880, 2840, 1645, 1620, 1595, 1395, 1328, 1105 cm^{-1}; mass spectrum, *m/z* (relative intensity) 180 (m^+, 15), 135 (100), 125 (39), 107 (35), 105 (30), 91 (44).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.72. Found: C, 73.56; H, 8.95.

(−)-2,7-Dimethyl-7-(methoxymethyl)cyclohepta-1,3,5-triene ((−)-1). A solution of crude 3,5-dimethyl-1,5-(methoxymethyl)-cyclohepta-2,6-dien-1-one (0.86 g, 59% pure, 2.8 mmol) in dry ether (60 mL) was cooled (0 °C) under a nitrogen atmosphere and treated with a 1.4 M hexane solution of diisobutylaluminum hydride (6.8 mL, 9.5 mmol). The resulting solution was stirred at 0 °C for 2.5 h, and then methanol (15 mL) was carefully added. The solids were removed by filtration and rinsed well with methanol; the combined filtrate and rinses were concentrated to yield 0.73 g of a cloudy oil. This oil and a catalytic amount of *p*-toluenesulfonic acid monohydrate were dissolved in dichloromethane (40 mL) and heated at reflux under a nitrogen atmosphere for 2.5 h. The reaction mixture was concentrated, and the residue was dissolved in ether (40 mL). This solution was washed (10% HCl, saturated $NaHCO_3$, brine), dried ($MgSO_4$), filtered, and concentrated to yield 0.56 g of the triene 1 as a light yellow liquid. Analysis by VPC on a 6.4 mm × 2.5 m 10% DBTCP on 60/80 Chromosorb W NAW column coupled with a 6.4 mm × 0.35 m 10% SE-30 on 60/80 Chromosorb W column at 120 °C showed this material to contain approximately 70% of the desired triene 1. The NMR and rotation samples were purified by using the conditions described above: $[\alpha]_{436}$ −7.7° (*c* 0.0073 g/mL, $CHCl_3$); NMR ($CDCl_3$) δ 0.96 (3 H, s), 1.93 (3 H, d, J = 1), 3.23 (2 H, s), 3.36 (3 H, s), 4.89 (1 H, s), 5.16 (1 H, d, J = 11), 5.96–6.40 (3 H, m); NMR (C_6D_6) 1.09 (3 H, s), 1.82 (3 H, d, J = 1.5), 3.11 (3 H, s), 3.14 (2 H, s), 4.97 (1 H, s), 5.23 (1 H, d, J = 10), 5.91–6.11 (1 H, m), 6.25 (2 H, m). This spectrum is comparable to the spectrum of the material prepared by Brassel:[14] NMR (60 MHz, C_6D_6) 1.07 (3 H, s), 1.81 (3 H, d, J = 1.5), 3.12 (5 H, s), 4.94 (1 H, s), 5.19 (1 H, d, J = 10), 5.98 (1 H, m), 6.2–6.25 (2 H, m).

The optical purity of this material was determined by NMR by employing tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III) and benzene-d_6 as the solvent. The shift reagent was added portrionwise until the C(7) methyl resonance split into two singlets at 3.33 and 3.36 ppm. The average of five integrations showed this material to be 16.2 ± 1.8% optically pure. The methyl resonance at δ 3.36 corresponded to the (−)-enantiomer.

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Registry No. (−)-1, 73992-48-0; (−)-**2**, 80721-88-6; (±)-**6**, 80721-89-7; **7**, 80721-90-0; **8**, 80721-91-1; (±)-**9**, 80721-92-2; (±)-**10**, 80721-93-3; (+)-**10**, 80721-94-4; (−)-**10**, 80721-95-5; (±)-**11**, 80721-96-6; (±)-**11** (−)-α-methylbenzylamine, 80721-97-7; **12**, 80721-98-8; **13**, 80737-52-6; **14**, 80721-99-9; **15**, 80722-00-5; **16**, 80722-01-6; **17**, 80722-02-7; **18**, 80722-03-8; **19**, 80722-04-9; **20**, 80722-05-0; **21**, 80722-06-1; **22**, 80722-07-2; **23**, 80722-08-3; **24**, 80722-09-4; 2-(trimethylsiloxy)buta-1,3-diene, 38053-91-7; 3-buten-2-one, 78-94-4; methyl methacrylate, 80-62-6.