Conjugate Addition of Methylmagnesium Iodide to 10-Methyl-1(9)-octal-2-one. An Approach to the Valeranone Carbon Framework

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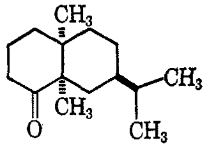
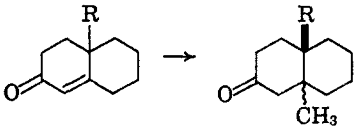
Methylmagnesium iodide, upon addition to 10-methyl-1(9)-octal-2-one (**1**) in the initial presence of cupric acetate, afforded as the sole 1,4 adduct, *cis*-9,10-dimethyl-2-decalone (**2a**), in 30–40% yield. The tertiary alcohol resulting from 1,2 addition comprised the remainder of the reaction product. The 1,4 adduct, decalone **2a**, was characterized through degradation to the previously reported compound, *cis*-1,2-dimethylcyclohexane-1,2-dicarboxylic anhydride (**8**). Neither 10β-methyl-7α-isopropyl-1(9)-octal-2-one (**12**) nor 10β-methyl-7α-isopropenyl-1(9)-octal-2-one (**11**) gave a 1,4 adduct with methylmagnesium iodide. Instead, the corresponding tertiary alcohols were obtained in high yield. A mechanistic interpretation is presented for the 1,4-addition reaction.

The structural peculiarities of the nonisoprenoid sesquiterpene valeranone have only recently been completely elaborated thanks to the combined efforts of British, Indian, Czech, and Japanese workers.[1] Valeranone, with its unusual arrangement of a methyl substituent at both carbon atoms comprising the decalin ring juncture, represents the first known member of a new class of sesquiterpenes. The structure elucidation of this natural product was hampered owing to the lack of known 9,10-dimethyldecalin derivatives of well-defined stereochemistry which could be used for comparison with valeranone degradation products. Because of their scarcity and because we were interested in synthetic approaches to valeranone, we considered various methods for constructing 9,10-dimethyldecalins.


valeranone

A potentially useful synthetic route to these compounds was first explored by Birch and Robinson, who utilized the cuprous bromide catalyzed reaction of 1(9)-octal-2-one (I) with methylmagnesium iodide to prepare *cis*-9-methyl-2-decalone (II), the product of conjugate addition, in 60% yield.[2] However, when applied to the homologous octalone, 10-methyl-1(9)-octal-2-one (**1**), the same reaction yielded mainly the unsaturated alcohol resulting from addition to the carbonyl grouping; the product of conjugate addition **2** was isolated in only 5% yield. Birch and Robinson regarded this latter substance as a mixture of stereoisomers on the basis of its broad melting range (90–95°). They felt that the angular methyl group of octalone **1** obstructed the approach of the Grignard reagent and suggested that the major 1,4-addition product was, therefore, most likely *trans*-9,10-dimethyl-2-decalone (**2b**). These findings evidently discouraged further work with angularly methylated octalones, such as **1**, until 1962 when Birch and Smith[3] reported that in tetrahydrofuran cupric acetate serves as a superior catalyst for a comparable addition reaction. Their report prompted us to investigate the conjugate methylation of octalone **1** under the improved conditions as a possible route to valeranone and related compounds.


I, R=H II, *cis*, R=H
1, R=CH_3 **2a**, *cis*; R=CH_3
2b, *trans*, R=CH_3

Our preliminary studies revealed that, for optimum yields of 1,4 adduct, a 0.2–0.3 molar ratio of cupric acetate to octalone **1** was needed. With this catalyst-octalone ratio, 9,10-dimethyl-2-decalone (**2**) comprised 40% of the product and the remainder consisted of alcoholic materials resulting from 1,2 addition. We found it interesting that an increase from 0.2 to 0.3 mole equiv of catalyst did not influence the ratio of 1,4 to 1,2 addition, but a similar increase from 0.1 to 0.2 mole equiv nearly doubled the percentage of 1,4 adduct **2**. This observation seems best reconciled by postulating limited solubility of the catalyst in the reaction medium with saturation being reached at about the 0.2 mole equiv level.

Decalone **2** could be easily separated from the alcoholic by-products through chromatography on alumina. The crystalline ketone thus obtained melted over a broad range (108–118°) even after numerous recrystallizations. However, this material appeared homogeneous by gas chromatography and the nmr spectrum displayed sharp peaks at 0.90 and 1.05 ppm due to the angular methyl groups. Its conversion to sharply melting semicarbazone and benzylidene derivatives in high yield, provided additional evidence for the homogeneity of this decalone. Ozonation of the latter derivative (**3**) gave the diacid **4**, also in high yield. Having thus ascertained that conjugate addition to octalone **1** followed a stereoselective pathway, we considered methods to establish the stereochemistry of the decalone (**2**) thereby obtained. For this objective, *cis*-1,2-dimethylcyclohexane-1,2-dicarboxylic anhydride (**8**),[4]

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(1) W. Klyne, S. C. Bhattacharyya, S. K. Paknikar, C. S. Narayanan, K. S. Kulkarni, J. Křepinský, M. Romaňuk, V. Herout, and F. Šorm, *Tetrahedron Letters*, **No. 23**, 1443 (1964), and references cited therein; H. Hikino, Y. Hikino, Y. Takeshita, K. Meguro, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **11**, 1207 (1963); for a recent stereoselective synthesis of this natural product, see J. A. Marshall, W. I. Fanta, and G. L. Bundy, *Tetrahedron Letters*, **No. 52**, 4807 (1965).

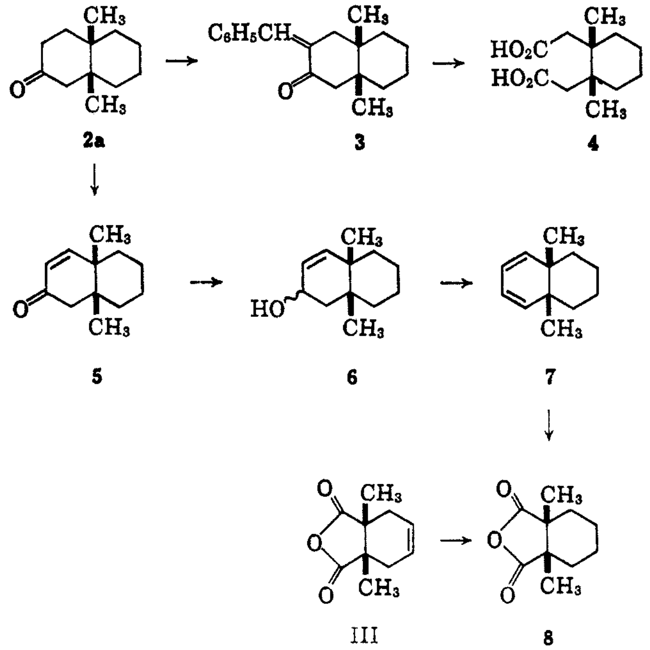
(2) A. J. Birch and R. Robinson, *J. Chem. Soc.*, 501 (1943). We repeated this experiment using conditions subsequently described in this paper and obtained a 1,4 adduct containing 99% of the *cis* isomer II in 80% yield.

(3) A. J. Birch and M. Smith, *Proc. Chem. Soc.*, 356 (1962).

(4) R. B. Woodward and R. B. Loftfield, *J. Am. Chem. Soc.*, **63**, 3167 (1941).

available from the Diels–Alder adduct III of 1,3-butadiene and dimethylmaleic anhydride, seemed a promising comparison substance. The requisite degradation of decalone 2 was carried out as shown in Chart I.

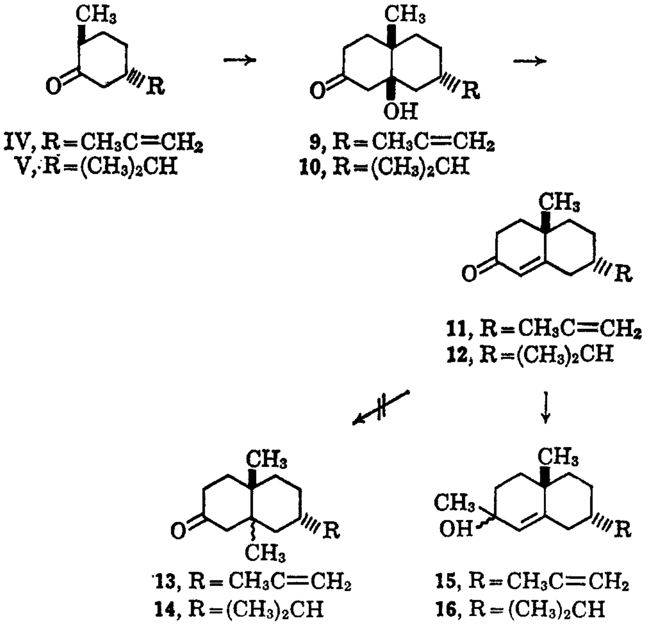
Chart I



Octalone 5 was prepared from decalone 2a by bromination in acetic acid and subsequent dehydrobromination of the crude bromo ketone with calcium carbonate in dimethylacetamide. The allylic alcohol 6, obtained by treating octalone 5 with lithium aluminum hydride, afforded diene 7 in high yield when heated in the presence of alkaline alumina. An intractable mixture of acidic materials resulted when ozone was used to oxidize diene 7, but the permanganate–periodate reagent of Lemieux and von Rudloff[5] gave satisfactory results. The crude acid thus secured afforded anhydride 8 upon prolonged exposure to refluxing acetyl chloride. This anhydride proved identical with that obtained from the Diels–Alder adduct III, thus showing that the stereoselective conjugate addition of methylmagnesium iodide to 10-methyl-1(9)-octal-2-one (1) gives the *cis* 1,4 adduct 2a and not the *trans* 1,4 adduct 2b originally suggested.[2] After establishing this point, we investigated applications of the 1,4-addition reaction to the synthesis of 9β,10β-dimethyl-7α-isopropyl-2-decalone (14), the antipode of a transformation product[1] of valeranone.

10β-Methyl-7α-isopropyl-1(9)-octal-2-one (12), the required starting material for this endeavor, had previously been prepared from (−)-tetrahydrocarvone (V) *via* the Wichterle reaction,[6] a method which utilizes 1,3-dichloro-2-butene as a methyl vinyl ketone equivalent. Djerassi and co-workers[6] were thus able to secure 12 in 25% over-all yield after purification *via* a protracted gradient elution chromatography step. Alternatively, they prepared this octalone by condensing V with 4-diethylamino-2-butanone. In our preparation of octalone 12 we employed a modified Robinson annelation method[7] and obtained the crystalline ketol 9 in 40% yield from (+)-dihydrocarvone (IV) and methyl vinyl ketone. Catalytic hydrogenation of this substance afforded the dihydro ketol 10 which gave octalone 12 in 94% yield upon treatment with aqueous oxalic acid. These transformations are outlined in Chart II.

Chart II



Octalone 12 gave none of the expected 1,4-addition product 14 upon treatment with methylmagnesium iodide under conditions comparable with those successfully employed for octalone 1. Infrared and nmr spectral analysis of the distilled product indicated only alcohol 16 had formed. Octalone 11, prepared by base-catalyzed dehydration of ketol 9, likewise failed to yield any significant quantity of 1,4 adduct 13. These findings suggest that the side chains of octalones 11 and 12 in some way block the respective conjugate addition reactions.

Figure 1 depicts a hypothetical reaction pathway for the 1,4-addition reactions of interest in the present study. Dreiding models show that a reagent approaching octalone I at the β position along the axis of the p orbital[8] encounters greater hindrance on the concave than the convex face because of the axial substituents (hydrogens) at C-5 and C-7. In this light, the stereoselective formation of *cis*-9-methyl-2-decalone (II) might conceivably be explained by a mechanism involving steric approach control to the carbon–carbon double bond.[9] With octalone 1, the angular methyl group presents a considerable obstacle to a reagent approaching the β position from the convex face. Consequently, this substance should give a substantially higher proportion of the *trans*-decalone product than octalone I if ground-state steric factors alone governed

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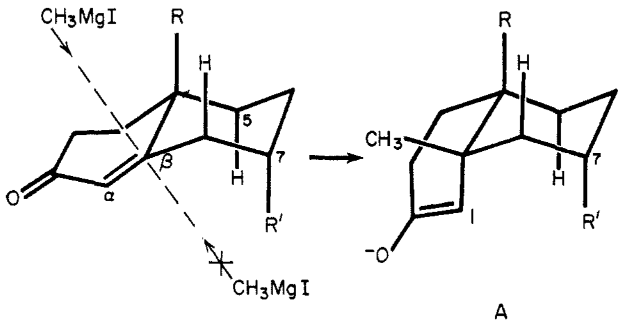
[5] R. U. Lemieux and E. von Rudloff, *Can. J. Chem.*, **33**, 1701 (1955).

[6] C. Djerassi, J. Burakevich, J. W. Chamberlin, D. Elad, T. Toda, and G. Stork, *J. Am. Chem. Soc.*, **86**, 465 (1964); J. A. Marshall and D. J. Schaeffer, *J. Org. Chem.*, **30**, 3642 (1965).

[7] J. A. Marshall and W. I. Fanta, *ibid.*, **29**, 2501 (1964).

[8] This type of stereoelectronic argument has been proposed for analogous 1,4-addition reactions. *Cf.* E. Toromanoff, *Bull. Soc. Chim. France*, 708 (1962).

[9] This concept (essentially a kinetic argument) has previously been used in conjunction with metal hydride reductions. *Cf.* W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Am. Chem. Soc.*, **78**, 2579 (1956).



I, R = R′ = H
1, R = CH_3; R′ = H
11, R = CH_3;
R′ = $CH_3C{=}CH_2$
12, R = CH_3;
R′ = $(CH_3)_2CH$

Figure 1.—Conjugate addition to 1,9-octal-2-ones.

the reaction (*i.e.*, kinetic control). This prediction is not born out by the experimental findings. Hence, some other factor must decide the course of the reaction with I and **1**. Stereoelectronic control, while an important factor in some conjugate addition reactions,[8] should not determine the stereochemistry here since optimum orbital geometry can be maintained en route to both *cis* and *trans* products, with octalones such as I and **1**, without the intervention of unfavorable ring conformations.

One satisfactory explanation for the observed results can be derived from the assumption that the transition state possesses, to some degree, the geometry of the enolate A (Figure 1). According to this mechanism, interactions between the angular methyl group and the incoming Grignard reagent (Figure 1, **1** → A) become less severe as the reaction progresses and the line of approach to the double bond more closely resembles an equatorial (to ring B) bond. If this explanation were fallacious and steric interactions in the developing product were inconsequential to the reaction progress, the yields of 1,4 adducts A [R = CH_3; R′ = H, R′ = $CH_3C{=}CH_2$, and R′ = $(CH_3)_2CH$] would be comparable since the convex face of each related octalone (**1**, **11**, and **12**) should be equally accessible. That this is not the case can be attributed to an increased activation energy for the latter (**11** → **13** and **12** → **14**) compared to the former (**1** → **2**) reactions and a corresponding preference for 1,2 addition, a reaction which should be virtually unaffected by substituents at C-7. By this argument then, conjugate addition to octalones **11** and **12** does not proceed because of the unfavorable transition-state interactions between C-1 and the axial substituents at C-5 and C-7. With octalones I and **1**, the interactions involving C-7 are considerably diminished and conjugate addition can occur with greater ease. Evidently interactions involving the incoming Grignard reagent and the angular methyl group of octalone **1** cannot be ignored. Otherwise 1,4 adducts II and **2a** would be formed in comparable yield.

Unfortunately, mechanistic considerations based on enolate A (Figure 1) do not seem to provide a generally satisfactory rationale for our observations. In particular, more of the *trans* isomer might be expected from octalones I and **1** if product stability alone governed the addition reaction. Kharasch and Reinmuth[10] suggested that the catalytic role of cuprous ion could involve coordination with the carbon–carbon double bond. If so, the ratio of *cis* to *trans* 1,4 adducts might be related to the stabilities of coordinated intermediates other than enolate **A**. This postulate receives support from the finding that cuprous bromide alters the ratio of stereoisomers obtained from 1,4 addition of phenylmagnesium bromide to (−)-menthyl crotonate.[11]

Experimental Section[12]

cis-**9,10-Dimethyl-2-decalone** (**2a**).—A solution of methylmagnesium iodide [from 2.88 g (0.12 g-atom) of magnesium turnings and 18 g of methyl iodide in 100 ml of ether] was cooled to −10° and a solution containing 6.56 g (0.04 mole) of 10-methyl-1(9)-octal-2-one (**1**)[7] and 2.08 g (0.01 mole) of cupric acetate monohydrate in 150 ml of dry tetrahydrofuran was added over 0.5 hr with efficient stirring.[12b] The dark mixture was allowed to warm to room temperature over 2 hr and was heated to reflux for 15 min. After treatment with excess aqueous ammonium chloride, the mixture was extracted with ether (The pale green aqueous phase became deep blue upon shaking in air.), and the combined organic layers were washed with aqueous sodium thiosulfate solution, brine, and dried over anhydrous sodium sulfate. Removal of the solvent afforded 7.4 g of yellow-brown oil: λ_{max}^{film} 2.91 (OH), 5.84 μ (ketone CO). The crude material was chromatographed on 450 ml of alumina and 2.90 g (40%) of dimethyldecalone **2a** was eluted with benzene and 5% ether in benzene. The gas chromatogram[13] indicated essentially one component.

This waxy, camphoraceous, semicrystalline material was crystallized from hexane at −78° giving 1.90 g (26%) of ketone **2a**: mp 108–118° (lit.[2] mp 90–95°); $\lambda_{max}^{CCl_4}$ 5.84 (ketone CO), 7.22, 8.05, 8.55, 9.93 μ; $\delta_{TMS}^{CCl_4}$ = 1.05 (CH_3), 0.90 ppm (CH_3). Gas chromatography indicated a purity of 98%.[13] Further recrystallization did not improve the melting point.

The semicarbazone derivative, mp 200–202° (lit.[2] mp 202–203°), was prepared in 77% yield from the recrystallized decalone.

Using a 0.1 molar ratio of cupric acetate to octalone **1** the yield of decalone **2**, as judged by the integrated nmr spectrum, was 25%.

The benzylidene derivative 3 was prepared from 0.54 g of decalone **2a** according to the procedure of Johnson.[14] The solid was filtered from the reaction mixture and crystallized from aqueous ethanol affording 0.70 g (87%) of white solid, mp 87–87.5°.

Anal. Calcd for $C_{19}H_{24}O$: C, 85.03; H, 9.01. Found: C, 85.15; H, 9.2.

The nmr spectrum of this derivative confirmed the assumption that the benzylidene grouping occupied the 3 position rather than the *a priori* less likely 1 position. The following peaks were observed: $\delta_{TMS}^{CCl_4}$ = 7.45 (C_6H_5CH) 6H, 2.84–2.30 (C-1 and C-4 protons) 4H, 1.52 (ring protons, sharp envelope) 8H, 1.01 ppm (angular CH_3) 6H.

cis-**1,2-Dimethylcyclohexane-1,2-diacetic Acid** (**4**).—Ozone was passed through a solution of 0.67 g of benzylidenedecalone **3** in 70 ml of ethyl acetate at −78° until the appearance of a persistent blue color. Acetic acid (10.5 ml) and 30% hydrogen peroxide (4 ml) were added and the solution was allowed to stand at room temperature for 48 hr. After the addition of 25 ml of ethyl acetate, the solution was washed with acidified aqueous

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[10] M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, p 220.

[11] Y. Inouye and H. M. Walborsky, *J. Org. Chem.*, **27**, 2706 (1962). For a conflicting result, see H. O. House and H. W. Thompson, *ibid.*, **28**, 360 (1963).

[12] (a) Melting points were determined on a Fisher-Johns hot stage. (b) The apparatus described by W. S. Johnson and W. P. Schneider [*Org. Syn.*, **30**, 18 (1950)] was used to maintain a nitrogen atmosphere. (c) The isolation procedure consisted of thorough extraction and back-extraction with the specified solvent, washing the combined extracts with saturated brine, and drying the extracts over anhydrous magnesium sulfate. The solvent was removed from the filtered extracts under reduced pressure on a steam bath. (d) Microanalyses were performed by Micro-Tech Laboratories, Inc., Skokie, Ill.

[13] A 13-ft, 16% Carbowax-20M on Diatoport S column at 210° was employed.

[14] W. S. Johnson, *J. Am. Chem. Soc.*, **65**, 1317 (1943).

ferrous sulfate until the washings remained pale green, and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was crystallized from ethyl acetate giving 0.45 (80%) of diacid, mp 216–216.5°. A second crop of 0.03 g (5%), mp 214.5–215.5°, was also obtained.

Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 62.9; H, 8.6.

cis-**9,10-Dimethyl-3-octal-2-one** (5).—A solution of 1.80 g of decalone **2a** in 20 ml of glacial acetic acid was cooled intermittently in ice, while 10.5 ml of 1 *M* bromine in glacial acetic acid was added over 15 min. The resulting bromo ketone mixture was isolated with ether[12c] after careful neutralization of the acetic acid with 10% aqueous sodium hydroxide. Removal of the solvent from the dried ethereal layers afforded 2.66 g (100%) of crude oily bromo ketone, $\lambda_{\max}^{\text{film}}$ 5.78 μ (ketone CO).

A solution of the crude bromo ketone and 2 g of calcium carbonate in 40 ml of N,N-dimethylacetamide contained in a 100-ml round-bottomed flask, fitted with a reflux condenser, was stirred at reflux under nitrogen[12b] for 45 min.[15] The cooled reaction mixture was filtered and the calcium carbonate pad washed well with hexane. The filtrate was diluted with an equal volume of hexane, swirled, and the layers separated. The N,N-dimethylacetamide layer was extracted with six additional portions of hexane, and the combined extracts were washed twice with saturated aqueous sodium bicarbonate solution, and once with water and brine. The extracts were dried over anhydrous magnesium sulfate and the solvent was removed at reduced pressure affording 1.81 g (100%) of red-brown ketone. Distillation gave 1.72 g (96%) of faint green, semicrystalline octalone **5**: bp 70–80° (bath temperature) at 0.06 mm; $\lambda_{\max}^{\text{film}}$ 5.95 (ketone CO), 6.15 (C=C), 7.18, 7.28, 7.90, 11.47, 12.39, 12.50, 12.99 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 6.53 (C-4 H; doublet, J = 10 cps), 5.87 (C-3 H; doublet, J = 10 cps), 2.24 (C-1 H), 1.08 (CH_3), 1.01 ppm (CH_3).

The analytical sample, mp 57–62°, $\lambda_{\max}^{\text{EtOH}}$ 232 mμ (ϵ 7600), was obtained by recrystallization at −78° from hexane and sublimation (55–65° at 0.05 mm).

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.8; H, 10.3.

The dinitrophenylhydrazone derivative, mp 161–162°, was prepared.

Anal. Calcd for $C_{18}H_{22}N_4O_4$: C, 60.32; H, 6.20; N, 15.63. Found: C, 60.5; H, 6.4; N, 15.6.

cis-**9,10-Dimethyl-1,3-hexalin** (7).—Solid lithium aluminum hydride (250 mg) was cautiously added, in small portions, to a solution of 1 g of octalone **5** in 40 ml of ether and the resulting mixture was stirred at room temperature for 4.5 hr. Water (0.5 ml) and 10% aqueous sodium hydroxide (0.4 ml) were carefully added and the mixture was stirred for eight additional hours. Filtration and removal of the solvent afforded 1.19 g (100%) of colorless alcohol **6**: $\lambda_{\max}^{\text{film}}$ 3.00 (OH), 6.05 (C=C), 9.38, 9.66, 9.81, 10.64, 13.23, 13.40 μ.

The dehydration procedure of Corey and Hortmann[16] was modified. A 10-ml test tube containing the crude allylic alcohol **6** and 3.2 g of neutral alumina (Woelm, activity I), which had previously been treated with pyridine, was immersed in an oil bath preheated to 230°. A slow stream of nitrogen was passed over the reaction mixture in order to carry the dehydration product into a −78° cold trap as it formed. After *ca.* 1 hr, heating was discontinued, and the contents of the trap were transferred, with the aid of anhydrous ether, to a flask containing anhydrous magnesium sulfate. The solvent was carefully removed from the dried ether layer by distillation at atmospheric pressure affording 820 mg (91%) of light yellow residue. This material was purified by passage through a chromatographic column containing 50 ml of Fisher alumina. Careful distillation of the pentane fraction (450 ml) afforded 774 mg (85%) of diene **7** as a colorless oil: $\lambda_{\max}^{\text{film}}$ 3.31 (vinyl H), 7.25, 13.00, 13.21, 14.25 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 5.83 (C-2 H, C-3 H; A_2B_2, 5-line pattern) 2H, 5.50 (C-1 *H*, C-4 *H*; A_2B_2, 5-line pattern) 2H, 1.41 (sharp) 8H, 0.92 ppm (CH_3) 6H.

The analytical sample, bp 70° (bath temperature) at 27 mm, $\lambda_{\max}^{\text{EtOH}}$ 262 mμ (ϵ 2900), was obtained by distillation.

Anal. Calcd for $C_{12}H_{18}$: C, 88.82; H, 11.18. Found: C, 88.6; H, 11.3.

cis-**1,2-Dimethylcyclohexane-1,2-dicarboxylic Anhydride** (8).—The procedure of Lemieux and von Rudloff[5] was employed. A 1000-ml, round-bottomed flask fitted with a Hershberg wire stirrer was charged with a mixture of 162 mg (1.0 mmole) of diene **7**, 0.83 g (6.0 mmoles) of potassium carbonate, 3.68 g (16.0 mmoles) of potassium periodate, and 42 mg (0.27 mmole) of potassium permanganate in 800 ml of water. After stirring rapidly at room temperature for 24 hr, the reaction mixture was extracted with four portions of ether to remove neutral material. The aqueous layer was acidified with hydrochloric acid and extracted with six portions of ether. The combined extracts were dried over anhydrous magnesium sulfate and the solvent was removed by distillation at atmospheric pressure giving 195 mg (97%) of red-brown acidic material: $\lambda_{\max}^{\text{film}}$ 2.80–4.20 (acid OH), 5.50–6.20 (acid CO), 9.51, 10.51, 11.37 μ.

The procedure of Woodward and Loftfield was followed.[4] A solution of the crude acid in 5 ml of acetyl chloride was heated to reflux under nitrogen for 20 hr.[12b] The acetyl chloride was removed by heating on a steam bath and the residual oil, $\lambda_{\max}^{\text{film}}$ 2.70–4.00 μ (acid OH), was dissolved in ether and washed with four portions of saturated aqueous sodium bicarbonate to remove acidic materials. The ether extracts were dried over anhydrous magnesium sulfate and the solvent was removed by distillation affording 100 mg of dark oil. Sublimation of this material gave 80 mg (44%) of anhydride **8**: $\lambda_{\max}^{\text{CCl}_4}$ 5.40, 5.60 (anhydride CO), 8.02, 8.41, 10.32, 10.60, 10.81, 11.17 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 1.38–2.14 (br) 8H, 1.25 ppm (CH_3) 6H.

This material, mp 115–120° after recrystallization from pentane at −78°, exhibited identical spectral properties (infrared, nmr) as *cis*-1,2-dimethylcyclohexane-1,2-dicarboxylic anhydride, mp 127–130° (lit.[4] mp 129°), prepared by the method of Woodward and Loftfield[4] from butadiene and dimethylmaleic anhydride.

(+)-**Dihydrocarvone** (IV).—A solution of 100 g (0.67 mole) of (+)-carvone in 830 ml of anhydrous ether was added over 3 hr to a solution of 18.7 g of lithium in 3 l. of distilled ammonia, after which 0.2 l. of absolute ethanol was added over 3.5 hr. After the addition of *ca.* 170 g of ammonium chloride, the ammonia was allowed to evaporate. The yellow residue was isolated with ether affording 96.4 g (95%) of a mixture of dihydrocarvone and dihydrocarvol. The crude mixture was dissolved in 700 ml of acetone (distilled from potassium permanganate), cooled to 0°, and treated over a 45-min period with Jones reagent[17] until a persistent red color developed (*ca.* 80 ml). Isopropyl alcohol was added to destroy the excess oxidizing agent, and the solution was neutralized with sodium bicarbonate. The mixture was filtered and the solid washed well with ether. Most of the acetone was removed from the filtrate at reduced pressure and the product was isolated with ether.[12c] Distillation gave 66.2 g (66%) of (+)-dihydrocarvone: bp 87–90° (5 mm) [lit.[18] bp 93° (14 mm)]; $\lambda_{\max}^{\text{film}}$ 5.84 (ketone CO), 6.08 μ (C=C).

10β-Methyl-7α-isopropenyl-9β-hydroxy-2-decalone (9).[19]—To 1.8 ml of 3 *N* ethanolic sodium ethoxide in 22.8 g (0.15 mole) of (+)-dihydrocarvone (IV) a solution of 22.8 g (0.15 mole) of (+)-dihydrocarvone and 10.5 g (0.15 mole) of methyl vinyl ketone was added over 5.5 hr.[12b] The reaction was stirred at −10° for 7.5 hr after addition. The organic material was isolated with ether; the residue was distilled affording three fractions: (1) 26.0 g (57% recovery) of (+)-dihydrocarvone, bp 84° (4.5 mm) to 68° (0.05 mm); (2) 19.3 g (58% yield) of ketols, bp 113–120° (0.07 mm); (3) 2.25 g (7%) of ketols, bp 120–124° (0.07 mm). Fractions 2 and 3 crystallized on standing and were recrystallized from ether–hexane affording 13.0 g (39%): mp 105–107°; $\lambda_{\max}^{\text{CCl}_4}$ 2.89 (OH), 5.84 (ketone CO), 6.09 (C=C), 9.90, 11.18 μ; $\delta_{\text{TMS}}^{\text{CHCl}_3}$ = 4.65 (C=CH_2), 2.54 (OH), 1.68 (C=CCH_3), 1.20 ppm (CH_3); ORD[20] in dioxane (c 0.20), $[M]_{589}$ −42°, $[M]_{316}$ +1050° (peak), $[M]_{310}$ +755° (sh), $[M]_{317}$ +715° (sh), $[M]_{305}$ +672° (sh), $[M]_{270}$ −2940° (trough). A second crop containing 0.75 g (2%), mp 101–104°, was isolated. The analytical sample, mp 106–107°, was obtained by further recrystallization from hexane.

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[15] Essentially the procedure of G. Green and A. Long [*J. Chem. Soc.*, 2532 (1961)].

[16] E. J. Corey and A. G. Hortmann, *J. Am. Chem. Soc.*, **85**, 4033 (1963).

[17] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

[18] G. Farges and A. Kergomard, *Bull. Soc. Chim. France*, 51 (1963).

[19] The stereochemistry is assigned on the basis of the ORD curve and degradation to 10β-methyl-7α-isopropyl-9β-decalol. This alcohol was independently synthesized by an unambiguous method as described in the Ph.D. Dissertation of W. I. Fanta, Northwestern University, 1965.

[20] We are indebted to Professor C. Djerassi for this determination.

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.8; H, 9.8.

10β-Methyl-7α-isopropyl-9β-hydroxy-2-decalone (10).—A solution of 7.76 g of ketol **9** in 70 ml of absolute ethanol was hydrogenated over 0.5 g of platinum oxide at 1 atm. Approximately 1 hr was required for the theoretical uptake of hydrogen. The catalyst was removed by filtration and the solvent was removed from the filtrate at reduced pressure. Distillation of the residue gave 7.03 g (90%) of ketol **10** as a colorless oil, bp 117° (0.2 mm) to 114° (0.1 mm), and 0.5 g (6%), bp 100–115° (bath temperature) at 0.05 mm (evaporative distillation of the residues). The material crystallized upon overnight refrigeration and was recrystallized from hexane at −78°. The material which could be recrystallized in 90% yield exhibited mp 52–56°; $\lambda_{max}^{CCl_4}$ 2.89 (OH), 5.85 (ketone CO), 7.80, 9.61, 9.94 μ; $\delta_{TMS}^{CCl_4}$ = 2.85 (O*H*), 1.19 (C*H*$_3$), 0.87 ppm (CHC*H*$_3$; doublet, *J* = 5 cps). The distilled material was found suitable for subsequent reactions. The analytical sample, mp 58–59°, was obtained by recrystallization from a small volume of hexane at −10°.

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.0; H, 10.8.

10β-Methyl-7α-isopropenyl-1(9)-octal-2-one (11).—A mixture of 500 mg of 10β-methyl-7α-isopropenyl-9β-hydroxy-2-decalone (**9**) and 5 ml of 10% aqueous potassium hydroxide solution was stirred at reflux under nitrogen for 8 hr[12b] and cooled; the product was isolated with ether.[12c] The crude octalone was distilled giving 436 mg (96%) of product: bp 85–95° (bath temperature) at 0.05 mm; λ_{max}^{film} 3.24 (vinyl H), 5.99 (ketone CO), 6.19 (C=C), 8.01, 11.19 μ. The analytical sample, λ_{max}^{EtOH} 245 mμ (ε 12,700), mp 35°, was obtained by recrystallization from hexane at −20°.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.86. Found: C, 82.5; H, 10.0.

The dinitrophenylhydrazone derivative, mp 133–134°, was prepared in 73% yield.

Anal. Calcd for $C_{20}H_{24}N_4O_4$: C, 62.48; H, 6.29; N, 14.57. Found: C, 62.8; H, 6.4; N, 14.4.

10β-Methyl-7α-isopropyl-1(9)-octal-2-one (12).—A mixture of 7.0 g (0.031 mole) of ketol **10** and 70 ml of 10% aqueous oxalic acid was heated at reflux under nitrogen[12b] for 5 hr and cooled; the product was isolated with ether.[12c] Distillation of the residue afforded 6.05 g (94%) of octalone **12**: bp 83–84° (0.07 mm); λ_{max}^{film} 6.00 (ketone CO), 6.20 (C=C), 7.92, 10.18, 11.65 μ; $\delta_{max}^{CCl_4}$ = 5.63 (C=CH), 1.28 (CH$_3$), 0.90 ppm (CHC*H*$_3$; doublet, *J* = 5 cps); λ_{max}^{EtOH} 242 mμ (ε 13,800) [lit.[6] 239 mμ (ε 16,100)]; [α]D +48° (*c* 0.23, dioxane)[20] {lit.[6] [α]D +65° (*c* 1.44, methanol)}. The 2,4-dinitrophenylhydrazone, mp 149–150°, was recrystallized from methanol–ethyl acetate. We did not observe the mp (195–197°) reported for this derivative.[6]

Anal. Calcd for $C_{20}H_{26}N_4O_4$: C, 62.16; H, 6.78; N, 14.50. Found: C, 62.4; H, 6.9; N, 14.65.

Vpc of octalone **12** on a 10-ft, 20% Carbowax 20M on Gaspack F column at 195° indicated that the material was over 90% pure. The infrared spectrum was superimposable with that of the material prepared by Djerassi, *et al.*[6,21]

Attempted 1,4 Addition of Methylmagnesium Iodide to Octalones 11 and 12.—The Grignard reagent, prepared from 1.08 g (50 mg-atoms) of magnesium turnings and 7 g of methyl iodide in 40 ml of anhydrous ether, was cooled to −10°, and a solution of 3.09 g (15 mmoles) of octalone **12** and 0.52 g (3 mmoles) of cupric acetate monohydrate in 56 ml of anhydrous tetrahydrofuran was added over 0.5 hr.[12b] The dark reaction mixture was allowed to warm to room temperature over 2 hr and was refluxed for 15 min. The cooled mixture was carefully treated with excess aqueous ammonium chloride and extracted thoroughly with ether. The pale green aqueous phase became deep blue upon shaking in air. The organic layer was washed with aqueous sodium thiosulfate, brine, and dried over anhydrous sodium sulfate. Removal of the solvent at reduced pressure afforded 3.19 g (96%) of yellow-green oil: λ_{max}^{film} 3.00 μ (OH); $\delta_{TMS}^{CCl_4}$ = 5.20 (C=CH), 3.09–3.43 (OH), 1.20 (C-10 CH$_3$), 1.11 (C-2 CH$_3$), 0.88 ppm (CHC*H*$_3$; doublet, *J* = 6 cps). The spectra indicated only a trace (5%) of saturated ketone carbonyl (5.85 μ). Evaporative distillation gave 2.81 g (85%) of 2,10β-dimethyl-7α-isopropyl-1(9)-octal-2-ol (**16**): bp 75–85° (bath temperature) at 0.25 mm; λ_{max}^{film} 3.00 (OH), 6.02 (C=C), 7.23, 7.32, 8.87, 9.14, 9.60, 9.95, and 10.61 μ. Chromatography of 1.0 g of distilled material on 100 ml of alumina (Fisher) afforded 0.75 g of alcohol mixture **16** which was distilled twice affording the analytical sample.

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.9; H, 11.7.

The experiment described above was repeated using 3.06 g of isopropenyloctalone **11** and 3.31 g of oil was obtained. The infrared spectrum of this substance showed a strong band at 3 μ (OH) but was devoid of bands in the 5.8-μ region expected for a cyclohexanone carbonyl and was therefore not investigated further.

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(21) We are indebted to Professor Djerassi for a copy of his spectrum.

Oxygenation of 1,10-Dimethyl-1(9)-octalin

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1,10-Dimethyl-1(9)-octalin (**4**), prepared from 1,10-dimethyl-1(9)-octal-2-one *via* the alcohol **2** and acetate **3**, was subjected to chemically and photochemically excited oxygen. The principal product, 1-methylene-*trans*-10-methyl-9-decalyl hydroperoxide (**5**), was characterized through its hydrogenation product, *cis*-1,10-dimethyl-*trans*-9-decalol (**13**), independently synthesized from 10-methyl-*trans*-1(9)-oxidodecalin (**19**) and methylmagnesium bromide. The oxygenation products were converted to a mixture of allylic alcohols by treatment with lithium aluminum hydride. Gas chromatography and nmr analysis indicated a similar mixture of products from both photosensitized and chemical oxygenation of olefin **4**.

In recent years, several naturally occurring sesquiterpenes possessing oxygen functions at bridgehead positions have been identified (*e.g.*, telekin,[1] β-agarofuran[2]). These compounds pose some intriguing synthetic problems whose solution we felt might be available, in part, through the selective photooxygenation[3] of appropriately substituted 1,10-dimethyl-1(9)-octalins. That such selectivity might indeed be possible first became evident during studies which culminated in the total synthesis of racemic alantolactone.[4] In the course of that work we found that unsaturated lactone I afforded allylic hydroperoxide II as the predominant photo-

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