Anal. Calcd for $C_{20}H_{32}O_5$: C, 68.15; H, 9.15. Found: C, 68.44; H, 9.32.

Registry No.—**1**, 29606-32-4; **2**, 29461-24-3; **4**, 37705-47-8; **5**, 37759-46-9; **6**, 29606-33-5; **7**, 37759-48-1; **8**, 37759-49-2; **9**, 37705-50-3; **10**, 29461-38-9; **11**, 29722-58-5; **12**, 37759-52-7; **13**, 37759-53-8; **15**, 37759-54-9; **16**, 37759-55-0; **17**, 37759-56-1; **18**, 37705-51-4; **20**, 26549-00-8; **21**, 37759-57-2; **23**, 37759-58-3; **24**, 37759-59-4; **25**, 29389-54-6; **32**, 37759-61-8.

Acknowledgments.—We are grateful to Professor E. Wenkert (Indiana University) for a helpful discussion and to the National Science Foundation (Grant No. GP-15,331) and Hoffmann-La Roche, Inc., for generous financial support.

Biogenetically Patterned Total Syntheses of (+)-Occidentalol and 7-Epi-(−)-occidentalol[1,2]

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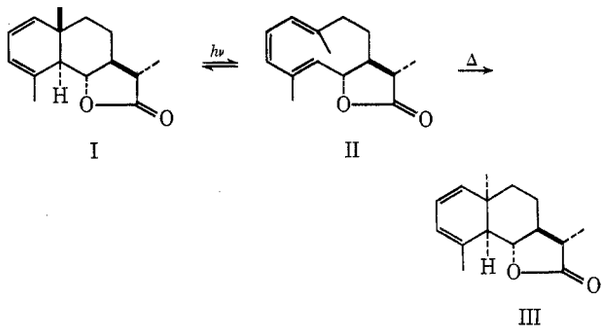
Diene (−)-**9** was prepared from (−)-**3** by standard procedures. Irradiation of **9** at −78° led to a probable photoequilibrium between **9** and an unstable intermediate believed to be **10**. Cyclodecatriene **10** underwent thermally induced cyclization at > −30° to yield cis-fused dienes (−)-**11** and (+)-**12** in a 2:1 ratio. The stereostructures assigned to the cis-fused dienes were based on conformational analysis, nmr, ORD, and CD data, and the finding that (−)-**11** is converted to (−)-**12** by base-catalyzed epimerization at C-7. Treatment of (+)-**12** with CH_3Li afforded (+)-occidentalol [(+)-**2**], thereby establishing the absolute stereostructure of this natural product. Similarly, (−)-**12** gave (−)-occidentalol [(−)-**2**] and (−)-**11** gave 7-epi-(−)-occidentalol [(+)-**1**]. A hypothetical biosynthetic scheme is outlined for the formation of (+)-occidentalol and some other known cis-fused eudesmanes by disrotatory cyclization of *trans,cis,trans*-cyclodecatrienes derivable from farnesol. A biogenetic-type synthesis of (+)-**2** and (+)-**1** *via* thermally induced cyclization of **15**, presumed to be generated during irradiation of (−)-**14**, is also described.

(+)-Occidentalol, a eudesmane-type sesquiterpene alcohol isolated from the wood of *Thuja occidentalis* L.[3,4] and *T. koraiensis* Nakai,[5] has been shown to have stereostructure (+)-**2**.[6] The coincident presence of a rarely occurring cis ring junction and a 1,3-diene system in occidentalol suggests that a unique biosynthetic pathway[7] involving disrotatory thermal cyclization[8] of a *trans,cis,trans*-cyclodecatriene intermediate derivable from farnesol may be operative in the formation of (+)-**2** and related cis-fused eudesmanes. We report here two total syntheses of (+)-**2** and (+)-**1** by routes (see Scheme I) which parallel the presumed biogenesis[7] and would seem to be generally applicable to the synthesis of other polyfunctionally substituted cis-fused decalins. A preparation of (−)-**2** from a common intermediate is also described.[9-11]

Total Synthesis and Stereochemistry of (+)-Occidentalol, (−)-Occidentalol, and 7-Epi-(−)-occidentalol



I II III

[(+)-**2**, (−)-**2**, and (+)-**1**].—The observation that thermally induced cyclization of cyclodecatriene II (generated by photolysis of I) affords cis-fused diene III[12] provided and experimental basis for the hypothetical biosynthetic scheme for (+)-**2** already outlined[7] as well as the biogenetically patterned syntheses of (+)-**2** shown in Scheme I.

Thus, keto ester (−)-**3**, prepared from (+)-carvone,[13] was brominated to yield the 2α-bromo derivative **4**. Dehydrobromination of crude **4** with LiBr and $LiCO_3$ in DMF at 120° gave the olefinic keto ester **5**, which could be purified by recrystallization of the corresponding acid, **6**, followed by remethylation of **6** with CH_2N_2 in ether. Reduction of either **5** or **6** with aluminum isopropoxide gave a mixture of olefinic hydroxy esters, **7** and **8**, *via* hydrolysis of the intermediate isopropyl ester analogs. Dehydration of the oily mixture of epimeric alcohols **7** and **8** by heating at 220° in the presence of alumina containing 2% pyridine[12] afforded the trans-fused diene **9** in ~25% yield. The diene **9** analyzed correctly for $C_{14}H_{20}O_2$ but contained 8–10%

(1) We thank the National Institutes of Health for financial support of this research (Grant GM13441).

(2) Reported in part at the 4th Midwest Regional Meeting of the American Chemical Society, Manhattan, Kans., Nov 1, 1968.

(3) (a) T. Nakatsuka and Y. Hirose, *Bull. Agr. Chem. Soc. Jap.*, **20**, 215 (1956); (b) *ibid.*, **23**, 140 (1959).

(4) E. von Rudloff and H. Erdtman, *Tetrahedron*, **18**, 1315 (1962).

(5) B. Tomita, Y. Hirose, and T. Nakatsuka, *J. Jap. Wood Res. Soc. (Mokuzai Gakkaishi)*, **15**, 76 (1969).

(6) A. G. Hortmann and J. B. DeRoos, *J. Org. Chem.*, **34**, 736 (1969), and references cited therein.

(7) A. G. Hortmann, *Tetrahedron Lett.*, 5785 (1968).

(8) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Verlag Chemie, Weinheim, Germany, 1970, pp. 38–64.

(9) Subsequent to our preliminary report of this work (ref 2) we were informed by Professor T. Asao (July 28, 1970) that his group has also prepared (+)-**1** and (−)-**2**: M. Ando, K. Nanaumi, T. Nakagawa, T. Asao, and K. Takase, *Tetrahedron Lett.*, 3891 (1970). Two unambiguous total syntheses of (+)-**2** have also been published recently; see ref 10 and 11. See also D. S. Watt and E. J. Corey, *Tetrahedron Lett.*, 4651 (1972), for a synthesis of (±)-**2**.

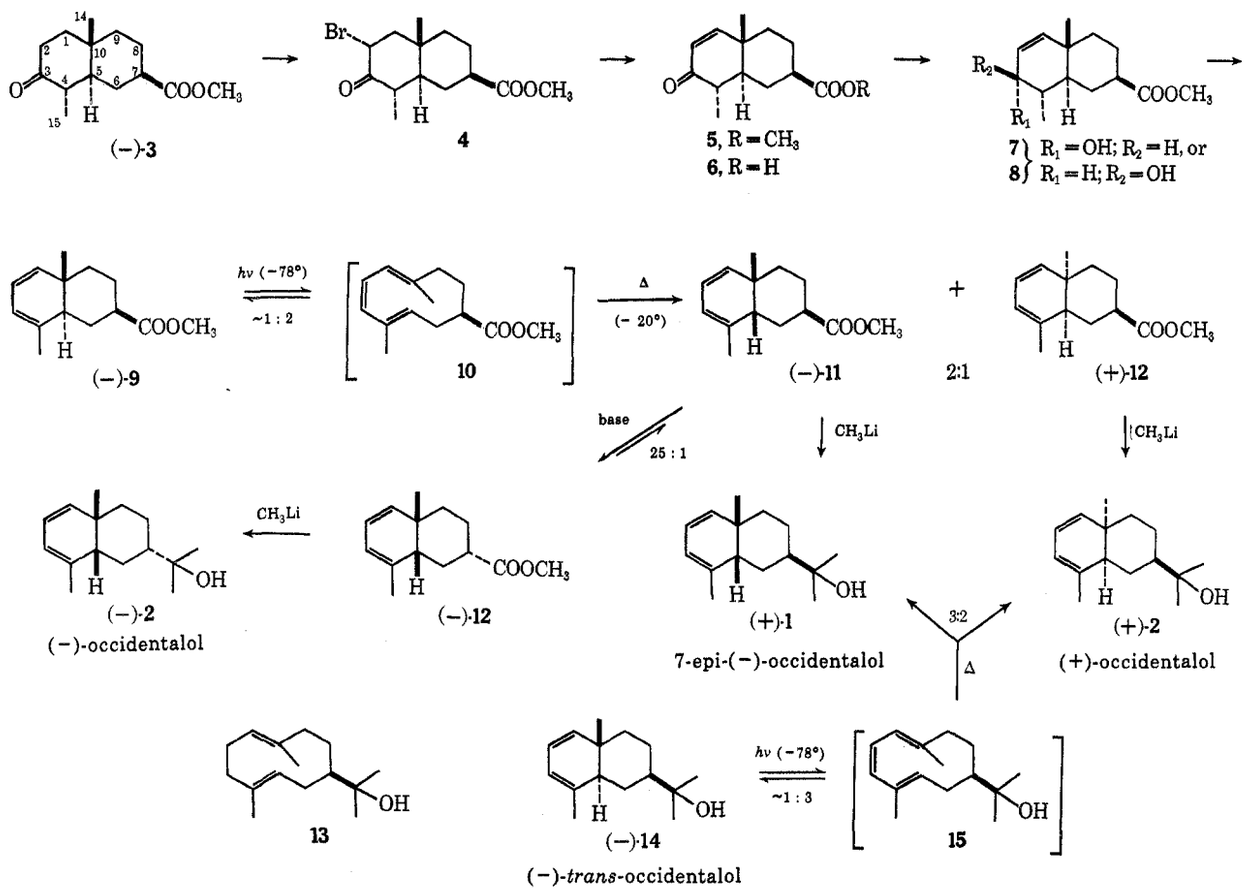
(10) M. Sergent, M. Mongrain, and P. Deslongchamps, *Can. J. Chem.*, **50**, 336 (1972).

(11) Y. Amano and C. H. Heathcock, *ibid.*, **50**, 340 (1972).

(12) E. J. Corey and A. G. Hortmann, *J. Amer. Chem. Soc.*, **85**, 4033 (1963); **87**, 5736 (1965).

(13) A. G. Hortmann, J. E. Martinelli, and Y. Wang, *J. Org. Chem.*, **34**, 732 (1969).

SCHEME I



of a major impurity (detectable by nmr analysis) which could not be removed by vpc, adsorption chromatography, or recrystallization of the acid corresponding to **9**. Subsequent attempts to prepare **9** in higher purity by heating pure **7**[14] at lower temperature (190°) in the presence of alumina containing 2% of quinoline afforded a similar yield of **9** which still contained 3–6% of the impurity mentioned above.[15]

The trans-fused diene **9** was irradiated in ether solution at −78° under an argon atmosphere using a small low-pressure mercury–argon discharge tube (Orien Optics Type C-13-61, 90% of output emitted at 2537 Å). Vpc analysis of aliquots withdrawn at 90–120-min intervals and warmed to 25° indicated the gradual appearance of two new peaks due to substances having greater mobility than **9** and shown by subsequent conversions (see below) to be cis-fused dienes **11** and **12** in a ratio of 2:1. A photostationary state was eventually reached at −78°, as evidenced by attainment of an approximately constant ratio (4:2:3) of **11**:**12**:**9** at 25°. On the basis of existing analogy,[12] *ca.* 33% of diene **9** remained in the steady-state mixture which resulted at −78°; similarly, the other component of the mixture at low temperature is considered to be triene **10**. Experiments in which the irradiation was monitored by uv spectroscopy at −70° provided support for the latter assumption. An increase in absorption at 222 and *ca.* 300 nm was found to occur as the absorption due to **9** at 266 nm steadily decreased during irradiation; warming aliquots of the irradiated solution prior to attainment of (or nearly at) the photostationary state, followed by recooling and redetermination of the spectrum, showed nearly complete restoration of the original absorption at 266 nm due to formation of **11** and **12** from **10**.[16,17] Observation of the rate of change in OD_{266} of the photolysis solution upon warming indicated that **10** had an approximate half-life of 15–30 min at −20°.

Continued irradiation at the photostationary state led to the gradual formation of at least three new substances (not further investigated) as evidenced by in-

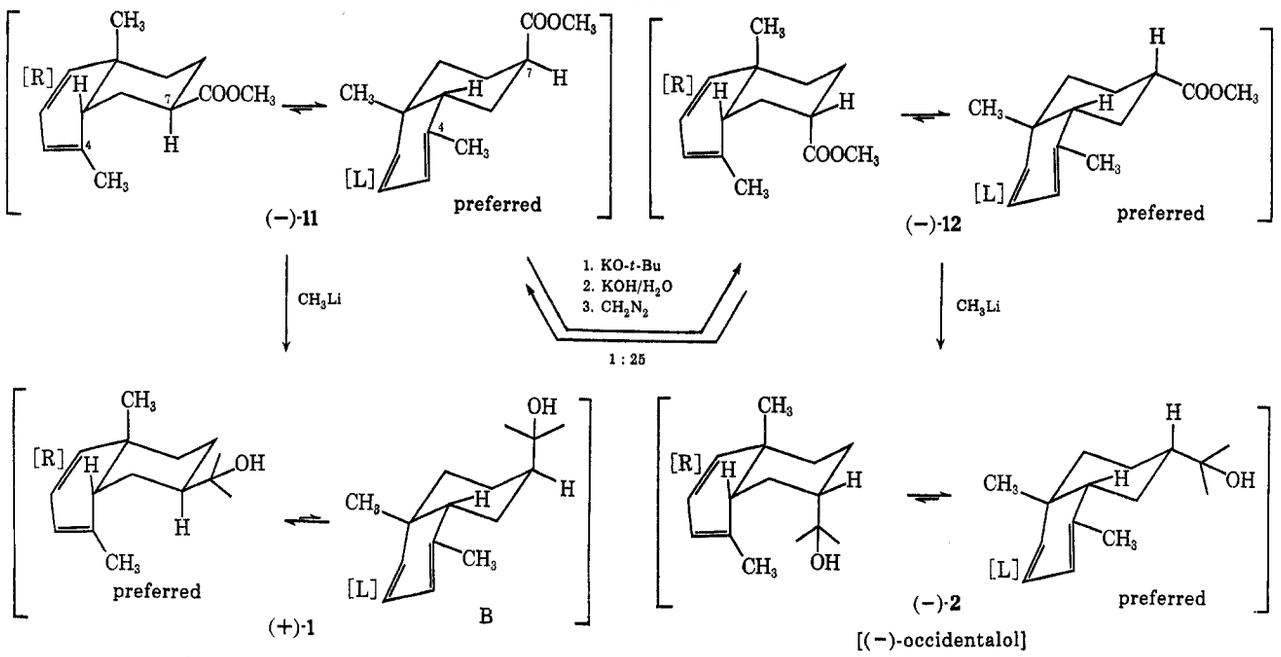
(14) The major isomer of the mixture of **7** and **8** could be crystallized in pure form and was arbitrarily designated as **7**. The configuration of **7** at C-3 was indeterminable.

(15) A possible structure for the impurity could be the $\Delta^{2,4}$ isomer of **9** which may be formed from **9** at elevated temperature by an allowed suprafacial 1,5 hydrogen shift. See R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, **87**, 2511 (1965); **88**, 2078 (1966); S. W. Staley and T. J. Henry, *ibid.*, **93**, 1292 (1971); H. C. Barrett and G. Büchi, *ibid.*, **89**, 5665 (1967). Attempts to prepare **9** at lower temperature (<150°) by pyrolysis of the 3,5-dinitrobenzoate of **7** [*cf.* A. W. Burgstahler and R. E. Sticker, *Tetrahedron*, **24**, 2435 (1968)], and by heating **7** with (carboxysulfamoyl)triethylammonium hydroxide inner salt methyl ester [*cf.* E. M. Burgess, H. R. Penton, Jr., and E. A. Taylor, *J. Amer. Chem. Soc.*, **90**, 4744 (1968) and references cited therein] gave less satisfactory results (see Experimental Section).

(16) However, upon warm up to 25° the absorption at 222 nm, which increased markedly during the irradiation, only receded to the extent of about 50% (see lines a, b, and b′ of Figure 1). Such behavior might be attributable to the presence of the $\Delta^{2,4}$ isomer of **9** (see ref 15). Photolysis of the $\Delta^{2,4}$ isomer of **9** would yield a ring-opened triene which would not recyclize at 25° and would be expected to have high end absorption and a somewhat more intense uv max than the $\Delta^{2,4}$ compound at *ca.* 260 nm; the latter absorption at 260 nm combined with a low-intensity maximum for **10** at *ca.* 280 nm[17] (note behavior at 300 nm, lines a, b, and b′ in Figure 1) would account for the observation that, whereas only 33% of **9** remains at the photostationary state (by vpc analysis of warmed solutions), OD_{265} is still 60% of the original value due to **9**.

(17) In addition to the uv max (MeOH) 211 nm (ϵ ~16,800) already reported[12] for II, a low-intensity uv max possibly arising from II at ~285 nm (ϵ < 2000) was also observed for solutions of I and II near the photostationary state (A. G. Hortmann, Ph.D. Thesis, Harvard University, 1964, p 40).

SCHEME II[a]



[a] Chirality of 1,3-diene system denoted by [R] or [L].

complete restoration of absorption at 266 nm upon warming to 25°, and by vpc analysis of the products obtained in earlier preparative experiments. In later preparative experiments, irradiation was halted prior to attainment of the photostationary state in order to simplify the vpc purification of **11** and **12** by minimizing the amounts of overirradiation products present.

A facile determination of the stereostructures of the two new dienes (**11**, $[\alpha]D$ −213°; **12**, $[\alpha]D$ +336°) obtained in the photolysis–recyclization sequence was effected by a study of their relative stabilities toward base-catalyzed epimerization at C-7. Treatment of the major diene [(−)-**11**] with potassium *tert*-butoxide, followed by hydrolysis of the resulting mixture of *tert*-butyl esters and methylation with CH_2N_2, afforded a mixture of methyl esters in a 25:1 ratio (nmr and vpc analysis). The minor component had the vpc mobility of the starting ester [(−)-**11**]; the major component had vpc retention time and ir and nmr spectra identical with those of **12**. Thus, **11** and **12** can only be cis-fused dienes, since epimerization of the only possible remaining diastereomer, the 7 epimer of the enantiomer of **9** (derivable by conrotatory photocyclization[8] of **10**) would have yielded the enantiomer of **9** under the epimerization conditions; similarly, (−)-**11** could be converted (*via* epimerization at C-7) only to the *enantiomer* of the minor diene (+)-**12** obtained in the photolysis–recyclization sequence.[18] Consequently, the ester (−)-**11** was assigned the stereostructure shown in Schemes I and II (two equatorial and two axial substituents on the B ring in chair form) on the basis of its observed epimerization to afford the more stable cis-fused structure [*i.e.*, (−)-**12**; three equatorial and one axial substituents on B ring].

Treatment of (−)-**11** with methyllithium afforded (+)-**1**, the structure which had been generally accepted[19] for (+)-occidentalol at the time that this work was in progress. Comparison of the ir and nmr spectra of synthetic (+)-**1** with spectra run on authentic (+)-occidentalol kindly supplied by Dr. E. von Rudloff clearly indicated that the two compounds were dissimilar. When, however, (+)-**12** was treated with CH_3Li, the synthetic (+)-**2** obtained was essentially identical in all respects with authentic (+)-occidentalol; similarly, treatment of (−)-**12** with CH_3Li afforded (−)-**2**, the enantiomer of natural occidentalol.[20]

These results led to a revision of the structure [(+)-**1**] previously accepted[19] for occidentalol to (+)-**2**, and were subsequently confirmed by a careful analysis of the 100-MHz nmr spectrum of (+)-**2**.[6]

Since this chemically based structural revision relied completely on the correctness of the structural assignments for cis-fused dienes **11** and **12**, several aspects of the nmr, CD, and ORD data for the esters and derived alcohols which vitiate any arguments for reversal of our original assignment of stereostructures to **11** and **12** deserve comment. In the vinyl H region of the nmr spectra (60 MHz) of **2**, **12**, and **11**, remarkably similar AMX patterns for H-1,2,3 are observed, whereas for **1** a complex ABC system is observed. In both alcohol **2** and ester **12** the nonsteroid conformations having their

(18) The conclusions rely on the reasonable assumption that epimerization at C-7 does not occur during photolysis of **9** or the recyclization of **10**.

(19) H. Ziffer, T. J. Batterham, U. Weiss, and E. von Rudloff, *Tetrahedron*, **20**, 67 (1964).

(20) The structural work described in this paper was originally undertaken on the assumption, based on optical data [K. Mislow and A. Moscowitz, *Tetrahedron Lett.*, 699 (1963)] and the reservations cited previously (see footnote 17 in ref 6), that (+)-**1** and (+)-**2** were *both* likely structures for (+)-occidentalol. Structure (−)-**1** was also considered as possible on the assumption that appreciable (yet minor) amounts of B′, the enantiomer of conformer B shown for (+)-**1** in Scheme II, in equilibrium with A′ might still give rise to a net positive Cotton effect. Although subsequent consideration of the absolute magnitude of the Cotton effect due to (+)-occidentalol seemed to weaken this argument (see discussion in ref 22), it is interesting to note, in retrospect, the contrast between $[\phi]_{286}$ +13,300 (extremum) for (+)-**1** and $[\phi]_{284}$ +43,000[19] for (+)-**2**.

10-CH_3 group and C-7 substituents equatorially oriented relative to ring B would be expected to be highly preferred;[6] thus, the nmr data suggest that **11** also prefers to exist in a nonsteroid conformation (see Scheme II). Support for this suggestion comes from the width at half-weight ($W_{1/2}$) of ~12 Hz observed for the resonance peak at δ 2.48 due to H-7 in **11** which is consistent with an equatorial orientation for H-7,[21] and from the ORD and CD curves of (−)-**11**, which show a strong negative Cotton effect consistent with a skewing of the cisoid butadiene in (−)-**11** in the sense of a left-handed helix.[22-24] Conversion of the 7-$COOCH_3$ group in (−)-**11** (axially oriented) to a more bulky 7-$CH(CH_3)_2$-OH group in (+)-**1** results, as would be expected, in an alteration of the nonsteroid conformation of **11** to that of the steroid type in **1** having its 10-CH_3 axially oriented and 7-$CH(CH_3)_2OH$ equatorially oriented;[23] conclusive support for this change in conformational preference in going from (−)-**11** to (+)-**1** comes from the ORD and CD curves of (+)-**1**, which exhibit a positive Cotton effect, indicating that the skew sense of the cisoid butadiene in (+)-**1** is that of a right-handed helix.[25] The strong conformational preferences assumed above for **12** and **2** and indicated in Scheme II were established by the observation of strong positive Cotton effects in the ORD and CD curves of (+)-**2** and (+)-**12**.[26]

The photolysis–recyclization sequence described above would appear to be specifically applicable to the synthesis of other known cis-fused eudesmanoid compounds incorporating either a 1,3-diene[24] or a Δ^1-3-ketone system;[27,28] more generally, it opens a route to polyfunctionally substituted cis decalins which originate from more readily available and predictably substituted trans decalins. Of additional interest is the finding that the *less stable* of the two possible cis-fused products is the predominant isomer formed in the thermally induced cyclization of **10**.

Of relevance to the photochemical studies described above are other recent studies of photoequilibria between 1,3-cyclohexadienes and 1,3,5-hexatrienes[29] and investigations of dihydronaphthalene–cyclodecapentene valence bond isomer systems.[30]

Biogenetic-Type Synthesis of (+)-1 and (+)-2.— Having established its absolute stereostructure, we turned our attention to a biogenetic-type synthesis[31] of (+)-occidentalol (**2**) modeled on its presumed biogenesis.[7] Generation of the required cyclodecatriene alcohol **15**, which in nature may be derived from "hedycaryol" (**13**),[32] was accomplished by photofission of diene (−)-**14** at −78° in a manner similar to that described for **9** → **10**. Irradiation was stopped when the system had reached the photostationary state. Warming the photolysis solution to 25° afforded a mixture of (+)-**2**, (+)-**1**, and **14** in a ratio of 6:9:5, respectively, thus providing direct experimental support for the plausibility of the postulated role of **15** in the biosynthesis of (+)-**2**.

The value of 1.5 found for [(+)-**1**/(+)-**2**] in the thermally induced cyclization of **15** is of particular interest in that it is very close to that found for [(+)-occidol (**20**)[33]/(+)-occidentalol (**2**)] in *T. occidentalis* (1.3)[34] and *T. koraienis* (1.7).[5] Since (+)-occidol (**20**) is a major constituent of the wood oil in both species (46% in the former, 12% in the latter), and since (+)-**1** is apparently not present in significant amount (if at all) in the oil of either, it is tempting to suggest that (+)-**20** arises in *Thuja* by an efficient conversion of any (+)-**1** formed *in vivo* by nonenzymatically controlled cyclization of **15**, whereas (+)-**2** formed *in vivo* from **15** remains unaltered.

An elaboration of the biogenetic scheme outlined previously[7] for the formation of cis-fused eudesmane-type sesquiterpenes, including the dehydrochamaecynenes (**18**)[24] and chamaecynones (**19**),[27] appears in Scheme III.[35] Also depicted is a novel suggestion due to Tomita and Hirose[36] for the formation (*via* **15** and **17**) of the unusual dihydrooxepin, (+)-occidenol (**21**),[5,36] which coexists with (+)-**2** and (+)-**20** in both *Thuja* species mentioned above.

Experimental Section[37]

3-Oxo-5,7αH,4βH-12,13-bisnoreudesm-1-en-11-oic Acid (6).— Keto ester (−)-**3**[13] (7.14 g, 0.030 mol) in 175 ml of $CHCl_3$ at 5° was treated with 4.92 g (0.031 mol) of Br_2 in 10 ml of CCl_4. The solution was stirred at room temperature until the orange

(21) See M. Karplus, *J. Amer. Chem. Soc.*, **85**, 2870 (1963).

(22) U. Weiss, H. Ziffer, and E. Charney, *Tetrahedron*, **21**, 3105 (1965).

(23) See ref 6 (footnote 11 and references cited therein) for a discussion of conformational preferences in other known examples of cis-fused eudesmanoid compounds, especially with regard to the orientation of C-7 substituents; see also ref 24.

(24) T. Asao, S. Ibe, K. Takase, Y. S. Cheng, and T. Nozoe, *Tetrahedron Lett.*, 3639 (1968).

(25) That such a conformational change had occurred was also suggested by a marked reversal noted in the vpc mobilities of **1** and **2** when compared with **11** and **12**, by the magnitude of $\Delta[\alpha]_D$ (*cf.* Mislow and Moscowitz in ref 20) noted in going from (−)-**11** to (+)-**1**, and by the differences in the vinyl H region of the nmr spectra of **1** *vs.* **2**, **11**, and **12** already mentioned.

(26) For (+)-**1** to correspond to (+)-occidentalol, as previously supposed (ref 19), would require that the photolysis–recyclization product having $[\alpha]_D$ +336° correspond in structure to that assigned in this work to (−)-**11**, and that this structure exist (to account for the large positive $[\alpha]_D$ and the strong positive Cotton effects observed in its ORD and CD curves) in a preferred conformation differing from that shown in Scheme II (which by itself seems plausible, although it makes nmr data cited for H-7 more difficult to rationalize). However, it then follows that the photolysis–recyclization product which has $[\alpha]_D$ − 213° must have the structure assigned in this work to (+)-**12**, and that this structure would have to exist in the clearly unfavorable conformation having one equatorial and three axial substituents on ring B in a chair form.

(27) T. Nozoe, Y. S. Cheng, and T. Toda, *Tetrahedron Lett.*, 3663 (1966); see also T. Nozoe, T. Asao, M. Ando, and K. Takase, *ibid.*, 2821 (1967).

(28) *Cf.* M. Miyashita, H. Uda, and A. Yoshikoshi, *Chem. Commun.*, 1396 (1969).

(29) W. G. Dauben, J. Rabinowitz, N. D. Vietmeyer, and P. H. Wendschuh, *J. Amer. Chem. Soc.*, **94**, 4285 (1972); W. G. Dauben and M. S. Kellogg, *ibid.*, **93**, 3805 (1971).

(30) S. Masamune and R. T. Seidner, *Chem. Commun.*, 542 (1969); S. Masamune, R. T. Seidner, H. Zenda, M. Wiesel, N. Nakatsuka, and G. Bigam, *J. Amer. Chem. Soc.*, **90**, 5286 (1968); E. E. van Tamelen, T. L. Burkoth, and R. H. Greeley, *ibid.*, **93**, 6120 (1971).

(31) E. E. van Tamelen, *Fortschr. Chem. Org. Naturst.*, **19**, 245 (1961).

(32) Isolation and synthesis of this biogenetically important sequiterpene have been reported: R. V. H. Jones and M. D. Sutherland, *Chem. Commun.*, 1229 (1968); 892 (1970); P. S. Wharton, C. E. Sundin, D. W. Johnson, and H. C. Kluender, *J. Org. Chem.*, **37**, 34 (1972).

(33) T.-L. Ho, *Can. J. Chem.*, **50**, 1098 (1972), and references cited therein.

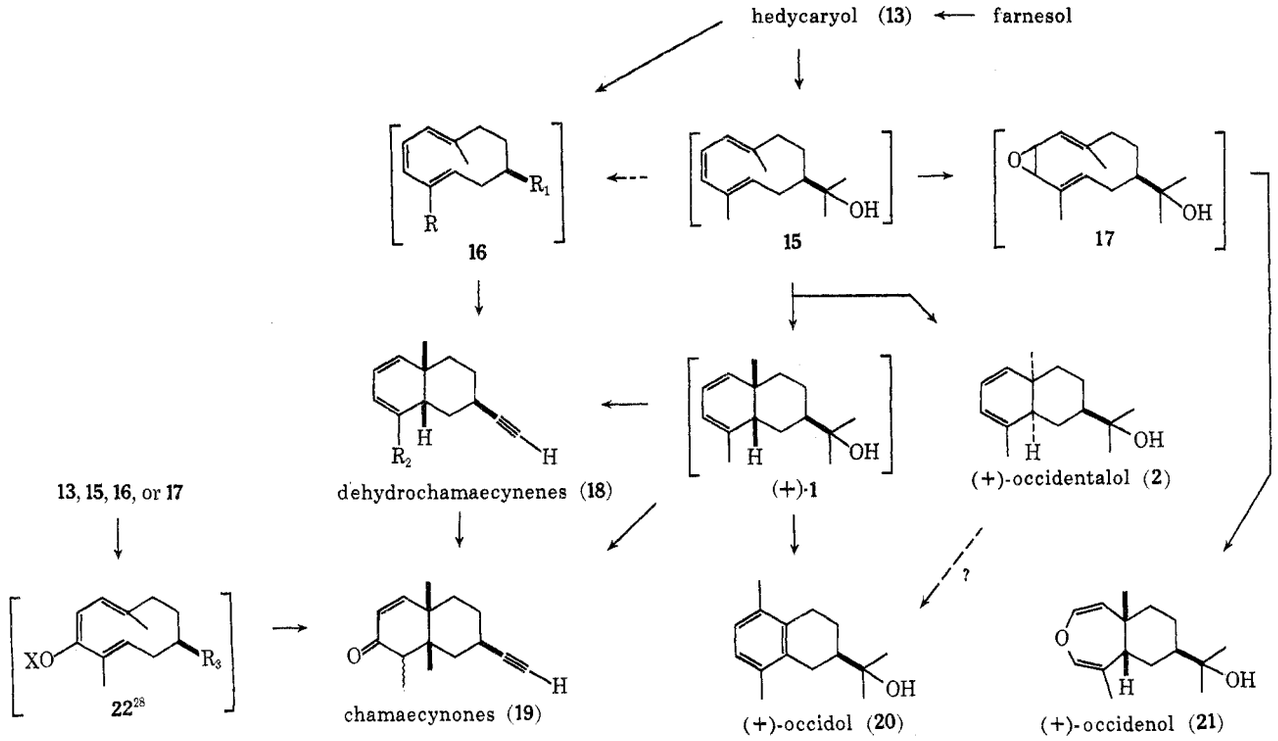
(34) E. von Rudloff and G. V. Nair, *ibid.*, **42**, 421 (1964).

(35) For a discussion of an alternative biosynthetic route to occidentalol (and occidol) see ref 34.

(36) B. Tomita and Y. Hirose, *Tetrahedron Lett.*, 235 (1970).

(37) All boiling points and melting points are uncorrected. Rotations were measured in $CHCl_3$. Infrared spectra were recorded in CCl_4 on a Perkin-Elmer Model 457 grating spectrophotometer. Mass spectra were determined using a Varian M-66 instrument; precise mass determinations have a precision of ±0.03 amu. Uv spectra were recorded in MeOH on Cary 11 and Cary 14 recording spectrophotometers. ORD and CD curves were measured in MeOH using a Durrum-Jasco Model J-20 spectropolarimeter; concentrations are stated in g/100 ml; only extreme values of ϕ and θ and locations of extrema are indicated. Nmr spectra were obtained for solutions in CCl_4 (unless stated otherwise) on a Varian A-60A spectrometer; peak positions are recorded in parts per million (δ) downfield from tetramethylsilane as an internal standard. Microanalyses were performed by Mikroanalytisches Laboratorium, Vienna, Austria.

SCHEME III



color disappeared (0.3 hr). After an additional 0.4 hr, the reaction mixture was poured into a separatory funnel and was washed successively with H_2O, 5% $NaHCO_3$ solution, and brine, dried ($MgSO_4$), and concentrated *in vacuo* at 25–35° to afford a yellow oil containing *ca.* 80 mol %[38] of **4**, the 2α-bromo derivative of **3**. The oil was dissolved in anhydrous DMF (75 ml) containing $LiCO_3$ (6 g) and LiBr (4.5 g). The suspension, in a round-bottom flask and under an atmosphere of N_2, was plunged into an oil bath at 135° and stirred rapidly for 1 hr while the temperature of the reaction mixture was maintained at 120–125°. The hot solution was poured into ice water containing ~3% HCl. The resulting mixture was extracted thoroughly with $CHCl_3$ (5 × 40 ml). A normal work-up procedure afforded an orange oil which was chromatographed on alumina (200 g, Woelm, neutral, activity grade ~I) packed in petroleum ether (bp 63–69°)–benzene (3:1). Elution with 2200 ml of the same solvent pair (2:3) afforded 5.08 g of pale yellow oil containing *ca.* 80% of methyl ester **5** by nmr assay. A solution of the oil in 75 ml of CH_3OH–H_2O (4:1) containing 5% KOH was stirred at room temperature for 20 hr, acidified with dilute HCl, and extracted with $CHCl_3$. The extracts were washed with brine, dried ($MgSO_4$), and concentrated to yield 3.78 g of crude **6** in several crops (mp 125–139°) on crystallization from CH_2Cl_2–petroleum ether. Recrystallization afforded 3.03 g (46%) of pure **6**, mp 138–140°. An analytical sample of **6** exhibited mp 141.5–142.5°; ir ($CHCl_3$) 3550–2450 (s, br), 1700, 1670, and 690 cm^{-1}; uv max 227 nm (ε 8610); nmr ($CDCl_3$) δ 1.13 (s, 3, H-14), 1.15 (d, 3, J = 6.7 Hz, H-15), 5.89 (d, 1, J = 10 Hz, H-2), 6.74 (d, 1, J = 10 Hz, H-1), and 11.90 (br s, 1, COOH).

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.32; H, 8.27.

The corresponding ester, **methyl 3-oxo-5,7αH,4βH-12,13-bisnoreudesm-1-en-11-oate (5)**, was obtained pure (nmr assay) and in quantitative yield on treatment of **6** with CH_2N_2 in Et_2O: mp 34–36°; nmr δ 1.06 (d, 3, $J \cong 7$ Hz, H-15), 1.12 (s, 3, H-14), 3.60 (s, $-OCH_3$), 5.68 (d, 1, J = 9.8 Hz, H-2), and 6.62 (d, 1, J = 9.8 Hz, H-1).

Methyl 3-Hydroxy-5,7αH,4βH-12,13-bisnoreudesm-1-en-11-oate (7) and Its C-3 Epimer (8).—A mixture of 1.033 g (0.0044 mol) of keto ester **5**, 3.04 g of freshly distilled aluminum isopropoxide, and 20 ml of anhydrous 2-propanol was heated at reflux for 4.3 hr; acetone, as it was formed, was slowly distilled through a Vigreux column and detected by formation of its 2,4-DNP derivative. The cooled mixture was poured into dilute HCl and extracted with ether. The ether extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to yield 1.25 g of the isopropyl ester analogs of **7** and **8** [nmr δ 1.20 (d, 6, J = 6.5 Hz) and 4.90 (septet, 1, J = 6.5 Hz)] as an oil. The oil was dissolved in CH_3OH–H_2O (4:1) containing 0.7% NaOH and the solution was refluxed for 3 hr under N_2, cooled, diluted with HCl, and extracted with Et_2O. A normal work-up followed by treatment of the acidic product with CH_2N_2 gave 0.95 g (91%) of a 3:1 mixture of isomeric hydroxy methyl esters **7** and **8** which crystallized partially to yield 0.30 g (29%) of the major isomer, **7** (pure by vpc),[39] as white needles: mp 90–91.5°; ir 3610, 3440 (s, br), and 1720 cm^{-1}; nmr ($CDCl_3$) δ 0.98 (s, 3, H-14), 1.03 (d, 3, $J \cong 7$ Hz, H-15), 1.78 (s, 1, –OH), 3.69 (s, 3, $-OCH_3$), ~3.69 (m, 1, H-3), and 5.53 (s, 2, H-1 and H-2). The mother liquor contained 0.60 g of **7** and **8** in a ratio of 3:2 as indicated by the relative peak areas for vinyl signals at δ 5.53 (s) and 5.69 (m, $W_{1/2}$ ~5 Hz).

Treatment of 0.33 g of the major isomer (**7**, mp 90–91.5°) with 3,5-dinitrobenzoyl chloride (4.11 g) in pyridine (25 ml) at 13° for 38 hr afforded, after several recrystallizations, 0.53 g (88%) of the 3,5-dinitrobenzoate of **7**: mp 185–187°; nmr ($CDCl_3$) δ 1.02 (d, 3, J = 6.5 Hz, H-15), 1.10 (s, 3, H-14), 3.69 (s, 3, $-OCH_3$), 5.25–5.90 (m, 3, ABC system, H-1,2,3), and 9.02 (m, 3, ArH).

(−)-Methyl 5,7αH-12,13-Bisnoreudesma-1,3-dien-11-oate (9). Method A.—Hydroxy ester **7** (mp 91–92.5°, 0.900 g, 0.0038 mol) was mixed with 5.4 g of alumina (Woelm, neutral activity grade ~I) that had been freshly treated with quinoline (2% by weight). The mixture was placed in a glass "boat" which was inserted into a preheated section of Pyrex tubing at 191° under an atmosphere of N_2 (flow rate ~160 ml/min).[12] The product slowly distilled from the alumina and condensed at the cool end of the tube as an oil (0.56 g) which was chromatographed on Florisil (14 g) to yield 0.25 g of crude diene **9** and 0.15 g of starting alcohol **7**. Two distillations of the diene in an evaporative still afforded 0.19 g (23%) of **9** as an oil: bp 34–39° (0.08 mm); uv max 264 nm (ε 4770); $[\alpha]^{25}D$ −55° (*c* 0.11); ir 1730 cm^{-1}; nmr δ 0.82 (s, 3, H-14), 1.77 (m, 3, $W_{1/2} \cong 3.5$ Hz, H-15), 3.62 (s, 3, $-OCH_3$), and 5.30–5.88 (m, 3, H-1,2,3). Diene **9** obtained in this manner contained 5–6% (nmr assay) of an impurity having a *C*-methyl (?) singlet at δ 0.93. The combined product ob-

(38) Determined by comparison of the area under the signal at δ 4.87 (dd, 1, $J_{2\beta,1\alpha}$ = 13.2 Hz, $J_{2\beta,1\beta}$ = 6.5 Hz, H-2β) with the total area under peaks due to $-OCH_3$.

(39) A 5 ft × 0.25 in. aluminum column containing 5% SE-52 on Anakrom ABS (60/70) was used for the analysis.

tained in 25% yield from two other identical runs contained 3–4% of the same impurity.

Method B.—Direct reduction of keto acid **6** (2.93 g) with aluminum isopropoxide in the manner described above for keto ester **5** afforded 2.00 g of hydroxy methyl esters **7** and **8** as a yellow oil after hydrolysis of the intermediate isopropyl esters and methylation of the crude hydroxy acids with CH_2N_2. The allylic alcohols were mixed with neutral alumina (12 g, pretreated with 2% pyridine) and pyrolyzed at 220° exactly as described previously[12] to afford 0.99 g of pale yellow oil. Chromatography on Florisil gave 0.77 g of colorless oil consisting of *ca.* 85% of diene **9**, 8–10% of a major impurity having a CCH_3 peak at δ 0.93 (see A), and several minor impurities (<2% of each by vpc analysis). Evaporative distillation afforded 0.687 g of **9** which was devoid of most minor impurities; a portion of the distilled material was sent for analysis.

Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.08; H, 9.36.

Extensive attempts to separate the diene **9** from the remaining major impurity (CCH_3 at δ 0.93) by glc, and tlc and column chromatography (including $AgNO_3/Al_2O_3$ and $AgNO_3/SiO_2$) failed.

Method C.—A mixture of 465 mg of the 3,5-dinitrobenzoate of **7** and 2.04 g of neutral alumina (Woelm, pretreated with 2% quinoline) was pyrolyzed at 174° as described in A. Florisil chromatography and evaporative distillation of the product gave 74 mg of an oil consisting of *ca.* 30% of diene **9** and at least four other unidentified methyl esters as determined by nmr analysis of the $-OCH_3$ region.

Method D.—A mixture of 147 mg of the 3,5-dinitrobenzoate of **7** and 2.9 g of base-washed sand was heated slowly to 150° (0.04 mm) in a short-path distillation apparatus. An oily solid (21 mg) having a complex nmr spectrum and containing no more (if any) than 5 mg of **9** condensed on the thermometer bulb. Washing the sand with $CHCl_3$ afforded 100 mg of a mixture of starting dinitrobenzoate and 3,5-dinitrobenzoic acid by nmr assay.

Method E.—(Carboxysulfamoyl)triethylammonium hydroxide inner salt methyl ester was prepared according to the procedure of Atkins and Burgess.[40] The inner salt (340 mg) was added to a solution of 130 mg (0.55 mmol) of allylic alcohol **7** in 15 ml of anhydrous benzene. The mixture was heated at 55° for 1 hr, cooled, diluted with Et_2O, washed with brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to leave 163 mg of oil. Chromatography on alumina followed by evaporative distillation afforded 30 mg (25%) of crude diene **9** contaminated with at least three other compounds [signals at δ 0.93 (~5%), 0.98 (~10%), and 1.07 (~5%)].

Photolysis of (−)-Methyl 5,7αH-12,13-Bisnoreudesma-1,3-dien-11-oate (9). Formation of (−)-11 and (+)-12.—The photolysis apparatus consisted of a Pyrex jacket (i.d. 59 mm) with side arm and fitted with a gas inlet tube at the bottom. A quartz Hanovia immersion well (o.d. 50.5 mm) was inserted into the Pyrex vessel. Irradiation was effected with an unshielded quartz low-pressure Hg–Argon discharge tube (Oriel Optics Type C-13-61; length 2.125 in., o.d. 6.5 mm; dissipated wattage *ca.* 4.6; 90% of output concentrated at 2537 Å)[41] powered by a 17-mA transformer (Oriel Optics Model C-73-16).

Run A.—A solution of 279 mg of diene **9** (prepared by method A) in 220 ml of anhydrous Et_2O was purged with ultrahigh-purity argon for 45 min, cooled to −78° in a Dry Ice–Et_2O bath, and purged for 20 min longer. After a short warm-up period the Hg–Argon lamp was suspended in the immersion well. Argon gas was continuously bubbled through the photolysis solution to provide agitation. The course of the reaction was followed by removing 2-ml aliquots with a syringe at 90-min intervals. The aliquots were warmed to room temperature, concentrated *in vacuo*, and assayed by vpc (5% SE-52; column 147°; head 185°).[39] As the ratio of peaks due to **11**, **12**, and **9** approached an approximately steady value previously determined to be about 4:2:3, the irradiation was stopped (420 min). The entire solution was warmed, concentrated *in vacuo*, and assayed by vpc, which indicated the presence of the same major components along with three very minor products, N, TT, and T (order of vpc mobility: **11**, N, **12**, TT, **9**, and T). The major components were separated by preparative vpc (10% XE-60; column 190°, head 210°)[42] to yield 96 mg of **11** (95% purity; contained N), 76 mg of **12** (60% purity; contained some **11** and N, and about 35% TT and **9**), and 71 mg of **9** (contained some TT and T). Rechromatography (vpc) of the first fraction (96 mg) afforded 50 mg (18%) of pure **(−)-methyl 7αH,5βH-12,13-bisnoreudesma-1,3-dien-11-oate** [(−)-**11**] as an oil: $[\alpha]^{25}D$ −213° (*c* 0.31); ir 1730, 1640, 1585, 1440, 1190, and 721 cm^{-1}; uv max 263 nm (ϵ 4900); ORD (*c* 0.00396) $[\phi]_{277}$ −28,200°, $[\phi]_{255}$ 0°, and $[\phi]_{230}$ +40,500°; CD (*c* 0.00396) $[\theta]_{258}$ −51,600° [lit.[9] CD (CH_3OH) $[\theta]_{259}$ −33,800°]; nmr δ 0.86 (s, 3, H-14), 1.80 (br s, 3, H-15), 2.48 (m, 1, $W_{1/2} \cong 12$ Hz, H-7), 3.64 (s, 3, $-OCH_3$), 5.22 (br d, 1, J = 9.5 Hz, H-1), 5.52 (br m, 1, H-3), and 5.79 (dd, 1, J = 9.5, 5.5 Hz, H-2); mass spectrum molecular ion theoretical 220.146, found 219.981.

Rechromatography (vpc) of the second fraction (76 mg) gave 45 mg (16%) of **(+)-methyl 5,7αH,10α-methyl-12,13-bisnoreudesma-1,3-dien-11-oate** [(+)-**12**] containing about 15% TT. Two additional passes afforded (+)-**12** of 95% purity (vpc) as an oil: $[\alpha]^{25}D$ +336° (*c* 0.43); ir 1733, 1645, 1587, 1445, and 722 cm^{-1}; uv max 264 nm (ϵ 4800); ORD (*c* 0.0035) $[\phi]_{281}$ +37,200°, $[\phi]_{262}$ 0°, and $[\phi]_{232}$ −62,000°; CD (*c* 0.0035) $[\theta]_{258}$ +75,300° (lit.[9] CD for (−)-**12**, $[\theta]_{262}$ −49,200°); nmr δ 0.87 (s, 3, H-14), 1.81 (br s, 3, H-15), 3.58 (s, 3, $-OCH_3$), 5.29 (br d, 1, J = 9.5 Hz, H-1), 5.57 (br d, 1, J = 5 Hz, H-3), and 5.84 (dd, 1, J = 9.5, 5 Hz, H-2); mass spectrum molecular ion theoretical 220.146, found 220.150.

Run B.—Diene **9** (400 mg, prepared by method B) was irradiated in two equal portions essentially as described above (run A) to yield, after the photolysis solutions were warmed, a mixture of **11**, **12**, and **9** in a ratio of ~2:1:1 along with N, TT, and T, totaling about 10–15% of the crude photolysis product. Separation by preparative vpc (10% XE-60)[42] afforded 85 mg of **11** (90–95% pure by vpc assay; contained N), 59 mg of a mixture of **12** (~50%), **11** (~20%), **9** (~10%), and smaller amounts of N and TT (determined by vpc assay and estimation of the areas of peaks due to $-OCH_3$ in **11**, **12**, and **9** at δ 3.64, 3.56, and 3.61, respectively), and 57 mg of a mixture of **9**, TT, and T.

Run C.—Diene **9** (606 mg in 580 ml of Et_2O; prepared by method B) was irradiated at −75° for 20 hr under argon using a larger Pyrex jacket (67-mm i.d.). Vpc analysis of the product obtained after the solution was allowed to warm to room temperature under argon showed the presence of **11**, **12**, and **9** in a ratio of 7:4:5. Repeated combination and repurification of fractions obtained by preparative vpc (10% XE-60)[42] afforded 110 mg of (−)-**11** (~98% purity) and 230 mg of a mixture of (−)-**11**, (+)-**12**, and **9** (~85%) of total material in a ratio of *ca.* 3:8:7.

Detection of Possible Photostationary State for 9 ⇌ 10 at −70°.—A solution of 16 mg of **9** (prepared by method B) in 210 ml of Et_2O was purged with argon and irradiated at −72 to −77° in the apparatus described above. Using a syringe which had been precooled in powdered Dry Ice, 8-ml aliquots were withdrawn at 0, 1.2, and 3.0 hr. The aliquots were transferred immediately to a precooled 1-cm quartz uv cell which was centered at the base of a small unsilvered quartz dewar and surrounded by Et_2O. The Et_2O in the dewar was maintained at −70 to −75° by addition of small chips of Dry Ice. The dewar (which was fitted near its base with two pairs of flat quartz windows at 180° to each other, and had a 2.2-cm path length between the inner faces of the inner windows) was secured by a custom-built cradle and placed in a Cary 11 uv spectrophotometer with its windows, and those of the enclosed uv cell, in the path of the sample beam. A base-line spectrum was previously run with pure Et_2O at −70 to −75° in the dewar and 1-cm cell, using two 1-cm cells filled with Et_2O at room temperature in the reference beam. The sample at t = 0 gave a spectrum of **9** at −70 to −75° having uv max 266 nm (ϵ 3000); the same sample of **9** in Et_2O at 25° exhibited uv max 265 nm (ϵ 4300). The sample withdrawn at 1.2-hr irradiation time showed uv max 268 nm (ϵ 1800), appearance of strong end absorption at 222 nm (ϵ 3440), and additional absorption at longer wavelength out to 340 nm (line b, Figure 1); warming the t = 1.2 hr aliquot to room temperature and recooling to −70 to −75° gave a spectrum (line b′) due to **11**, **12**, and **9**, having absorption intensity at ~265 nm, similar to that of starting diene **9**. The aliquot withdrawn at t = 3.0 hr showed a spectrum (line c) similar to that obtained after 1.2 hr, but with somewhat reduced end absorption at 222

(40) G. M. Atkins, Jr., and E. M. Burgess, *J. Amer. Chem. Soc.*, **90**, 4744 (1968).

(41) Oriel Optics Corp., Stamford, Conn. 06901.

(42) A 12 ft × 0.375 in. aluminum column containing 10% XE-60 on Anakrom ABS (60/70) was used.

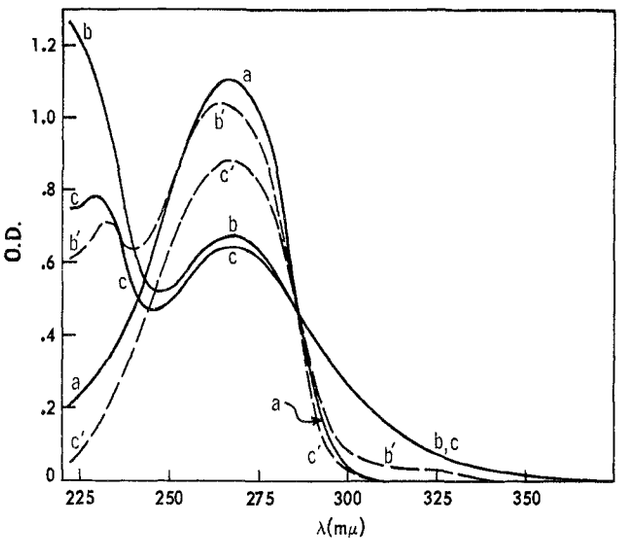


Figure 1.—Irradiation of 9 at −72 to −77°. All spectra were measured at −70 to −75°: (a) solution of 9 at $t = 0$; (b) irradiated solution of 9 at $t = 1.2$ hr (photostationary state for 9 ⇌ 10 approximately attained; (b′) solution b after warming to 25° and recooling; (c) irradiated solution of 9 at $t = 3.0$ hr; (c′) solution c after warming to 25° and recooling.

nm; warming and recooling led to regeneration of 80% of the approximate absorption expected at 265 nm if the final solution was composed solely of eudesma-1,3-dienes (*i.e.*, 11, 12, and 9).[43] Triene 10 at −70° could be estimated to have uv max at ~215 nm (ε ~500) and ~280 (~2200) by consideration of the differences in the b and b′ lines of Figure 1 and the assumption that 9 and 10 are present in a ratio of ~1:2 after 1.2-hr irradiation time (based on the ratio of 9 to 11 + 12 observed after warming solutions near the photostationary state in large-scale irradiations). Vpc analysis of the oil obtained after warming and concentrating the bulk of the photolysis solution after 3.0 hr irradiation time showed the presence of 11, 12, and 9 in a ratio of ~2:1:1 along with appreciable amounts of impurities (*e.g.*, N, T, and TT) typically formed when irradiation is continued at the photostationary state.

Estimation of the Half-Life of 10 at −20°.—The transparent quartz dewar used in the above uv determinations was fitted with a head to which was attached a tube which extended two-thirds of the way to the base of the dewar (*i.e.*, above the windows) and protruded from the top of the head. A side arm used as a nitrogen inlet was located near the top of the tube; a nitrogen outlet tube was located in the head. A 1-cm quartz uv cell having a long tube attached at its mouth was positioned with its windows facing the inside windows of the dewar; the tube attached to the uv cell traversed the inside of the tube attached to the head with enough clearance for two thermocouple wires which were fitted between the two tubes and attached at their termini to one side-wall of the uv cell (one at the top of the cell and one at the bottom). The same Hg–Ar lamp used in the irradiations of 9 described above was attached to the outside of the quartz dewar opposite the remaining side wall of the cell. The cell tube and thermocouple wires were fixed with a gas-tight seal to the top of the head tube. The open end of the cell tube was fitted with an ampoule cap and a long syringe needle which served as an argon inlet for both purging and agitating a solution contained in the cell; a short syringe needle served as an argon outlet. The entire unit was secured in the sample beam of a Cary 11 spectrophotometer by a custom-built cradle and the nitrogen inlet was attached to a tube leading to a 10-l. storage dewar containing liquid N_2 and fitted with a gas-tight head; a small heating element controlled by a rheostat was suspended in the N_2 from the head and allowed the boiling rate of the N_2 to be varied.

A solution of 9 (11.8 mg/100 ml) was injected into the uv cell and purged with argon. Agitation with argon was continued as the solution was cooled to −40 to −60° by circulation of cold N_2 gas which was forced through the system by increasing the boiling rate of the liquid N_2 in the reservoir. The solution was irradiated for 7-min intervals (3 ×) until the original OD at 260–270 nm was reduced by about one-third; the OD was measured after shutting off the lamp and withdrawing the argon inlet needle from the solution. No significant change in OD_{265} occurred as the solution was held at temperatures up to −30°; upon warming the solution above −30°, the OD_{265} increased at a rate consistent with a half-life for 10 of approximately 15–30 min at −20°.

Base-Catalyzed Isomerization of (−)-11 to (−)-12.—A solution of 95 mg of (−)-11 (84 mg from photolysis run B and 11 mg from earlier runs; contained ~5% of N) in 17 ml of anhydrous *tert*-butyl alcohol containing 0.68 g of potassium *tert*-butoxide was heated at reflux for 2.2 hr under N_2. Water (4 ml) was added and refluxing was continued for 3.8 hr longer. The cooled solution was diluted with cold HCl (10%) and extracted thoroughly with $CHCl_3$. The extracts were washed with brine, dried ($MgSO_4$), filtered, concentrated *in vacuo* at room temperature, treated with CH_2N_2 in Et_2O, and evaporated to dryness *in vacuo* to yield 88 mg of oil which consisted of (−)-12 and (−)-11 in a ratio of 25:1 by vpc analysis (10% XE-60; column 173°, head 184°; retention times 12, 14.7 min; 11, 10.2 min);[42] an impurity (5–6%) having the retention time of N (11.1 min) was also present. Pure (−)-12 (37 mg) was obtained as an oil by preparative vpc (10% XE-60);[42] uv max 263 nm (ε 4530); ir and nmr spectra identical with those of (+)-12 obtained by photolysis of 9.

(−)-11-Hydroxy-5,7βH,10β-methyleudesma-1,3-diene [(−)-2] [(−)-Occidentalol].—A solution of 35 mg of (−)-12 from the base-catalyzed isomerization of (−)-11 described above was treated with CH_3Li in Et_2O to yield 38 mg of semicrystalline material. Sublimation at 0.1 mm gave a pale yellow glass ($[\alpha]^{25}D$ −219°) containing 70–80% of 2 by nmr and vpc assay. Preparative vpc (10% XE-60)[42] afforded 10.2 mg of >90% pure (−)-2; mp 83–86°; $[\alpha]^{27}D$ −329° (*c* 0.33); uv max 263.5 nm (ε 5520); ir essentially identical with that of authentic (+)-occidentalol; vpc assay indicated 5–10% of a minor impurity having slightly longer retention time than (−)-2; no nmr was run. Repurification of 5.1 mg of the product by vpc on a 12 ft × 0.25 in. 10% XE-60 analytical column gave (−)-occidentalol: mp 93.8–94.8°; $[\alpha]^{27}D$ −356° (*c* 0.15); uv max 263.5 nm (ε 3960).

(+)-11-Hydroxy-5,7αH,10α-methyleudesma-1,3-diene [(+)-2] [(+)-Occidentalol]. A.—A solution of (+)-12 (35 mg in 1 ml Et_2O) from photolysis run A was treated with methyllithium (2 ml, 2.3 *M* in Et_2O) under N_2 at 0°. A normal work-up procedure gave 30 mg (86%) of an oil having an nmr spectrum essentially identical with that of authentic (+)-occidentalol.[6] Vpc assay (5% SE-52)[39] indicated the presence of 89% (+)-occidentalol (2) and 11% of three additional minor components in the oil. Purification by preparative vpc (XE-60, column 169°, head 204°)[42] gave 10.8 mg of crystalline material which was repurified by vpc to yield 5 mg of (+)-occidentalol (2) as fine needles: mp 92.5–94° (lit.[3a,4,10] mp 95°, 97.5–98°, 95°); $[\alpha]^{25}D$ +334° (*c* 0.16) [lit.[3a,4,10] $[\alpha]^{24}D$ +361° (*c* 2.4, $CHCl_3$), $[\alpha]^{25}D$ +363.2° (*c* 1.6, $CHCl_3$), $[\alpha]_{578}$ +369° ($CHCl_3$)]; uv max 264 nm (ε 4720) [lit.[3a] uv max 266 nm (ε 3980)]; ORD (*c* 0.0032) $[\phi]_{282}$ +38,700°, $[\phi]_{262}$ 0°, $[\phi]_{237}$ −54,500° [lit.[44] ORD (*c* 0.026, MeOH) $[\phi]_{284}$ +43,000°, $[\phi]_{240}$ −85,000°)]; CD (*c* 0.0032) $[\theta]_{260}$ +74,000° [lit.[44] CD (*c* 0.0026, EtOH) $[\theta]_{263}$ +66,260°].

B.—An ethereal solution of 59 mg of the vpc fraction containing 12, 11, and 9 obtained from photolysis run B was treated with excess CH_3Li. Work-up afforded 65 mg of a semicrystalline gum which contained *ca.* 50% (+)-occidentalol (2) and 15–25% of 1 by vpc analysis. [The order of mobility of the esters (−)-11 and (+)-12 was reversed in the corresponding alcohols 1 and 2, thus facilitating the purification of (+)-occidentalol (2) prepared in this manner from impure (+)-12; the ester (+)-12 can be purified only with considerable difficulty and losses of material.] Preparative vpc (10% XE-60)[42] afforded 21.2 mg of (+)-occidentalol (2): mp 79–85°; $[\alpha]^{25}D$ +301° (*c* 0.34, $CHCl_3$); uv max 262.5 nm (ε 5900). Two further purifications of 17.6

(43) Since the solutions could be run only after the last trace of Dry Ice in the Et_2O coolant was consumed (*i.e.*, after CO_2 bubbling ceased), the solutions tended to warm up slowly (to −55 to −65°) while the spectrum was recorded. Consequently, the solutions were recooled and the spectra were recorded several times for each aliquot to assure that any variation on OD values due to temperature changes were within reasonable limits; OD values near 265 nm were within ±0.05 of those shown in Figure 1 for each rerun. It should also be noted that the attenuation of OD noted for 9 in going from 25° to −70° may vary for the other species in solution, thus rendering any quantitation of results of dubious value.

(44) E. von Rudloff, cited in ref 22.

mg of the product by vpc gave 7.4 mg of partially crystalline material having mp 93.5–95.5° (softens at 91°). Sublimation gave (+)-occidentalol (**2**) having mp 94.2–95.0°; uv max 263.5 nm (ε 4300, 3940); $[\alpha]^{26}D$ +364°, +360° (*c* 0.36, $CHCl_3$). The nmr (microcavity tube) and ir spectra of synthetic (+)-occidentalol were essentially identical with spectra determined on a sample of authentic (+)-occidentalol (kindly supplied by Dr. E. von Rudloff) which exhibited mp 94–95.5°; $[\alpha]^{26}D$ +341° (*c* 0.53); uv max 263.5 nm (ε 4450).

C.—Treatment of the mixture (230 mg) containing **(+)-12** (*ca.* 86 mg) from photolysis run C with CH_3Li in Et_2O followed by preparative vpc afforded 35 mg of (+)-occidentalol (**2**), $[\alpha]^{27}D$ +290° (*c* 2.92); vpc showed ≥85% purity. Further purification of 29.2 mg of **(+)-2** by vpc gave 14.7 mg of a partly crystalline glass, $[\alpha]^{25}D$ +352° (*c* 0.19, $CHCl_3$). Sublimation of the glassy material gave (+)-occidentalol (**2**) as needles, mp 91.0–92.5°, uv max 264 nm (ε 3905).

(+)-11-Hydroxy-5β,7αH-eudesma-1,3-diene [(+)-1] [7-Epi-(−)-occidentalol].—A solution of **(−)-11** (40 mg from run A in 2 ml of Et_2O at 0°) was treated with methyllithium (1 ml of 2.3 *M* solution in Et_2O) under N_2. A normal work-up gave an oil which was purified by glpc (XE-60, column 190°, head 216°)[42] to yield 28 mg (70%) of **(+)-1** as a viscous liquid: $[\alpha]^{25}D$ +60.7° (*c* 0.15); uv max 266 nm (ε 4900) and 273 (shoulder); ORD (*c* 0.0029) $[\phi]_{286}$ +13,300°, $[\phi]_{263}$ 0°, $[\phi]_{234}$ −28,300°; CD (*c* 0.0029) $[\theta]_{261}$ +27,600°, $[\theta]_{270}$ +24,500° (shoulder), and inflections at 255 and 285 nm; nmr δ 1.10 (s, 3, H-14), 1.14 (s, 6, H-12 and H-13), 1.81 (br s, 3, H-15), and 5.1–5.8 (m, 3, H-1,2,3); mass spectrum molecular ion theoretical 220.182, found 220.170.

(−)-11-Hydroxy-5,7αH-eudesma-1,3-diene [(−)-14] [(−)-*trans*-Occidentalol].—A solution of 191 mg (0.87 mmol) of diene **9** (prepared by method A) in 10 ml of Et_2O was treated with 5 ml of 2.3 *M* methyllithium in Et_2O. The mixture was poured into ice water and worked up in the normal manner to yield 187 mg (98%) of solid. Recrystallization from hexane afforded 81 mg (42%) of (−)-*trans*-occidentalol (**14**) as white needles: mp 94–95.5°; $[\alpha]^{25}D$ −47° (*c* 0.32); ir ($CHCl_3$) 3620, 3480, 1645, and 1590 cm^{-1}; uv max 264 nm (ε 4700); ORD (*c* 0.0043) $[\phi]_{272}$ −8100°, $[\phi]_{255}$ 0°, $[\phi]_{225}$ +25,000°; CD (*c* 0.0043) $[\theta]_{250}$ −21,400°, $[\theta]_{210}$ +7200°; nmr ($CDCl_3$) δ 0.79 (s, 3, H-14), 1.22 (s, 6, H-12 and H-13), 1.38 (s, 1, OH), 1.80 (d, 3, *J* = 1.4 Hz, H-15), and 5.39–5.98 (m, 3, H-1,2,3).

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98; mol wt, 220.183. Found: C, 81.85; H, 10.86; mol wt, 220.203 (mass spectrum).

Photolysis of (−)-*trans*-Occidentalol [(−)-14].—A solution of trans-fused alcohol **(−)-14** (110 mg) in 270 ml of deoxygenated Et_2O at −78° was irradiated (4.1 hr)[45] as described above for the diene **9** (run A). Warm up (25°) and concentration of the solution afforded 115 mg of oil which consisted of (+)-occidentalol (**2**) (30%), 7-epi-(−)-occidentalol [(+)-**1**] (44%), (−)-*trans*-occidentalol (**14**) (24%), and a minor impurity (2%) as determined by vpc analysis on 10% XE-60[42] (column 190°, head 220°; retention times—**2**, 15.9 min; **1**, 20.9 min; **14**, 23.6 min; impurity, 28.0 min).

Registry No.—(+)-**1**, 29484-47-7; (−)-**2**, 29484-46-6; (+)-**2**, 473-17-6; (−)-**3**, 18508-76-4; **4**, 37573-94-7; **5**, 37573-95-8; **6**, 37573-96-9; **7**, 37573-97-0; **7** (3,5-DNB), 37573-98-1; **8**, 37573-99-2; **9**, 37574-00-8; (−)-**11**, 29484-53-5; (+)-**12**, 37574-02-0; (−)-**14**, 37574-03-1.

Acknowledgment.—We thank Professor S. I. Weissman for a loan of equipment for the low-temperature uv experiments.

(45) Preliminary experiments (see footnote 9 in ref 7) indicated that the photostationary state was probably achieved after about 3.7 hr.

Conformational Isomerism in Dihydropregeijerene and Hedycaryol[1,2]

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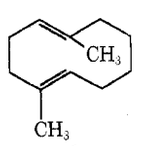
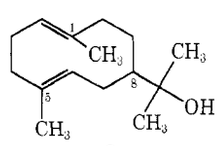
Conformations available to the 1,5-dimethyl-*trans,trans*-1,5-cyclodecadiene sesquiterpenes dihydropregeijerene (**1**) and hedycaryol (**2**) are discussed in terms of the cubic array of Chart 1. Conformers have either a crossed or parallel relation of the double bonds in association with arrangements of the C-7,8,9,10 methylene segment which are described as chair, twist–boat, and twists. They are interconverted by three processes: rotation of each of the double bonds through the ring and inversion of the C-8,9 unit. Variable-temperature nmr spectra of **1** and **2**, particularly of samples deuterated at C-2, were helpful in assessing conformer populations and interconversions. All interconversions rates are rapid at 90°; all are slow at −30°. The conformational compositions of both **1** and **2** consist of a mixture of crossed chair and approximately equal amounts of parallel twists *T′* and *T″* with a temperature-dependent composition favoring the parallel set at higher temperatures. However, the relative amounts of the crossed and parallel sets differ for the two molecules: for **1** the parallel set increases from 15% at −70° to 35% at 0°; for **2** the parallel set already predominates to the extent of 75% at −30°. The demonstration of the existence of specific conformers of hedycaryol provides an experimental basis for biogenetic speculations which have invoked stereospecific, conformationally controlled reactions.

Since 1959 many sesquiterpene *trans,trans*-1,5-cyclodecadienes (members of the germacrane class) have been isolated. Following the establishment of constitution and configuration, data have started to accumulate on conformations and their relation to reactivity, an area of considerable biogenetic importance.[3] This article provides data pertinent to the conformations in solution of two of the simplest sesquiterpene *trans,trans*-1,5-cyclodecadienes, dihydropregeijerene (**1**) and hedycaryol (**2**).



1



2

Hedycaryol is the simplest known representative of sesquiterpene *trans,trans*-1,5-cyclodecadienes which contain one or more chiral centers (in hedycaryol at C-8) in addition to the potential chirality of the ring system itself. Dihydropregeijerene is an even simpler molecule, lacking any chiral center and indeed any substitu-

(1) The investigation was supported by Public Health Service Research Grant GM 16338 from the Division of General Medical Sciences, U. S. Public Health Service.

(2) The article is abstracted from the Ph.D. theses of Y. C. P. and H. C. K., Wesleyan University, 1971.

(3) For a review see W. Parker, J. S. Roberts, and R. Ramage, *Quart. Rev., Chem. Soc.*, **21**, 321 (1967). The earliest significant speculation is that of J. B. Hendrickson, *Tetrahedron*, **7**, 82 (1959).