Experiments Directed toward the Total Synthesis of Terpenes. V. The Synthesis of the (±)-9-Isopimaradienes[1,2]

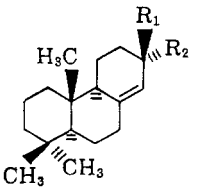
ROBERT F. CHURCH[3] AND ROBERT E. IRELAND

Department of Chemistry, The University of Michigan, Ann Arbor, Michigan

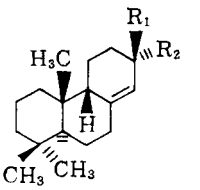
Received August 14, 1962

The *trans-syn-cis* ketone **14** has been synthesized *via* the pyrolytic rearrangement of the vinyl ether **9**. Conversion of this ketone **14** to the (±)-9-isopimaradienes **3** and **4** has been accomplished by methylation of the aldehyde **16**. The diene **3** is shown to be different from isopimaradiene and the diene **4** from rimuene. A new structure is proposed for isopimaric acid and, hence, isopimaradiene.

The synthesis[4] of (±)-sandaracopimaradiene (**1**) and (±)-pimaradiene (**2**) served to establish methods suitable for the elaboration of the ring C substitution pattern of the pimaric acids. With these methods available to us, it was natural to consider the synthesis of the remaining representative of the pimaric acids—namely, isopimaric acid. Again it seemed wise to restrict our



1. $R_1 = -CH_3$; $R_2 = -CH{=}CH_2$.
2. $R_1 = -CH{=}CH_2$; $R_2 = -CH_3$.



3. $R_1 = -CH_3$; $R_2 = -CH{=}CH_2$.
4. $R_1 = -CH{=}CH_2$; $R_2 = -CH_3$.

initial efforts to the hydrocarbon isopimaradiene (**3**), lacking as it does the asymmetry and functionality at C-4.

The structure and stereochemistry of isopimaric acid—and hence isopimaradiene (**3**)—has been the subject of extensive investigations beginning with its isolation in 1948 by Harris and Sanderson.[5] While in retrospect it is an easy matter to find flaws in the reasoning used to arrive at the structure **3**, at the outset the universal agreement of these investigators appeared to leave little doubt that the isopimaric acid system did indeed contain the interesting *trans-syn*-$\Delta^{8(14)}$-dodecahydrophenanthrene system shown. It was not until our synthetic work was nearly finished that it became apparent that this was not the correct structure. Thus a project that began as a test of modern synthetic methods became in the end a means for determining the structure of the natural product—a more classical result that one might not think necessary with the tools available today for structure determination.

As if to heighten the intrigue already inherent in this project, midway through our work Wenkert and Beak[6] reported that their spectral findings established that the diterpenoid hydrocarbon rimuene[7] had the stereochemistry shown in structure **4**. While such a structure was an obvious candidate for rimuene when the dienes[4,6] related to the three naturally occurring resin acids were ruled out, there are obvious flaws in this reasoning that Wenkert and Beak chose to ignore. Thus rimuene is quite stable toward mineral acid catalyzed isomerization,[7] while isopimaric acid [as well as isopimaradiene (*vide infra*)] is the most labile[5b,e] of the resin acids toward this treatment. Such a result can hardly be attributed solely to a change in stereochemistry at C–13. Similarly, inspection of even the small portion of the n.m.r. spectrum of rimuene reported by Wenkert and Beak[6] reveals a broad signal centered at 4.64 τ due to the nuclear vinyl hydrogen. The breadth of this signal is clearly inconsistent with the $\Delta^{8(14)}$-structure proposed by these workers, as the C-14-vinyl hydrogen cannot be strongly spin-coupled, lacking, as it does, any adjacent protons. Thus, it seemed unlikely that the stereochemical assignment made by these workers was correct even before our synthesis of the isomeric dienes **3** and **4** was complete.

Another point that was overlooked by Wenkert and Beak[6] and foreshadowed our results relative to the isopimaric acid structure was the clearly resolved doublet due to the nuclear vinyl hydrogen in the n.m.r. spectrum of methyl isopimarate. For the reasons stated above, such a signal could not be due to a C-14-vinyl hydrogen and was the first indication we had that the structure of isopimaric acid (and hence, isopimaradiene), too, was incorrect.

The key to the synthesis of the 9-isopimaradienes **3** and **4** was the construction of the *trans-syn-cis* ketone **14**.[8] Since the ketone **14** could not be obtained by any obvious modification of the synthesis used earlier for the isomeric *trans-anti-trans* ketone,[4] we were in need of a new route to the phenanthrene system. The opportunity to explore such a route presented itself as a result of our experiments[9] in connection with the Claisen rearrangement of the allyl vinyl ether **5**. It was previously shown[9] that the aldehyde obtained by the pyrolysis of the ether **5** possessed the α-(axial)-oriented acetaldehyde residue. This information opened the

(1) For a preliminary account of this work, see R. F. Church and R. E. Ireland, *Tetrahedron Letters*, 493 (1961); taken in part from the Ph.D. thesis of R. F. Church, University of Michigan, 1961.

(2) This work was supported in part by a Research Grant H-4179 from the National Heart Institute, National Institutes of Health.

(3) Dow Chemical Company Fellow, 1958–1959; Sun Oil Company Fellow, 1959–1960.

(4) R. E. Ireland and P. W. Schiess, *J. Org. Chem.*, **28**, 6 (1963).

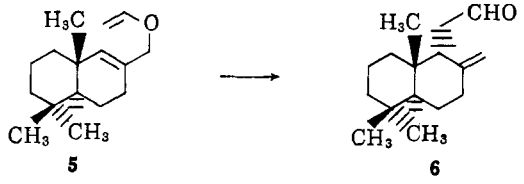
(5) (a) G. C. Harris and T. F. Sanderson, *J. Am. Chem. Soc.*, **70**, 2081 (1948); (b) O. E. Edwards and R. Howe, *Can. J. Chem.*, **37**, 760 (1959); (c) O. E. Edwards and R. Howe, *Chem. Ind.* (London), 537 (1959); (d) E. Wenkert and J. W. Chamberlin, *J. Am. Chem. Soc.*, **81**, 688 (1959); (e) B. Green, A. Harris, and W. B. Whalley, *J. Chem. Soc.*, 4715 (1958); (f) A. K. Bose, *Chem. Ind.* (London), 1105 (1960); (g) H. H. Bruun, *Acta Acad. Aboensis, Math. et Phys.*, **19** (3), 7 (1954); (h) H. H. Bruun, *Finska Kemistsamfundets Medd.*, **63**, 22 (1954); (i) H. H. Bruun, *Acta Chem. Scand.*, **6**, 798 (1952); (j) H. H. Bruun, I. Fishmeister, and E. Stenhagen, *ibid.*, **13**, 379 (1959); (k) H. H. Bruun, R. Ryage, and E. Stenhagen, *ibid.*, **12**, 789 (1958); (l) Le-van-Thoi and J. Ourgand, *Bull. soc. chim. France*, 202 (1956); (m) G. W. A. Milne and H. Smith, *Chem. Ind.* (London), 1307 (1961).

(6) E. Wenkert and P. Beak, *J. Am. Chem. Soc.*, **83**, 998 (1961).

(7) L. H. Briggs, B. F. Cain, and R. C. Cambie, *Tetrahedron Letters*, No. **8** 17 (1959).

(8) Since completion of our work, two other reports of the synthesis of related *trans-syn-cis*-perhydrophenanthrene systems have appeared: S. K. Balasubramanian, *Tetrahedron*, **12**, 196 (1961), and E. Wenkert, V. I. Stenberg, and P. Beak, *J. Am. Chem. Soc.*, **83**, 2320 (1961).

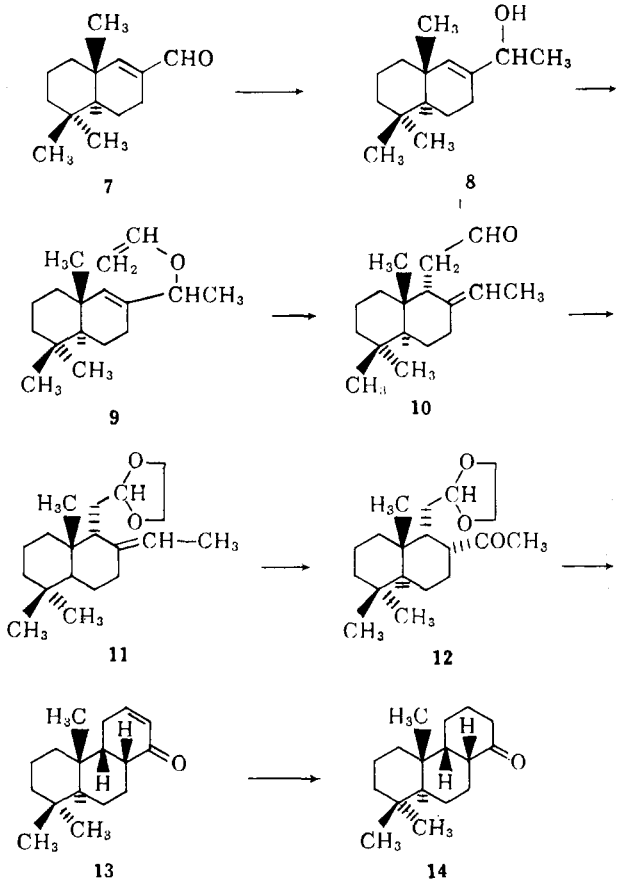
(9) R. F. Church, R. E. Ireland, and J. A. Marshall, *J. Org. Chem.*, **27**, 1118 (1962).



5 6

way to the construction of an analogous system with the desired *syn* relationship between the C_{10}—CH_3 and the C_9—H.

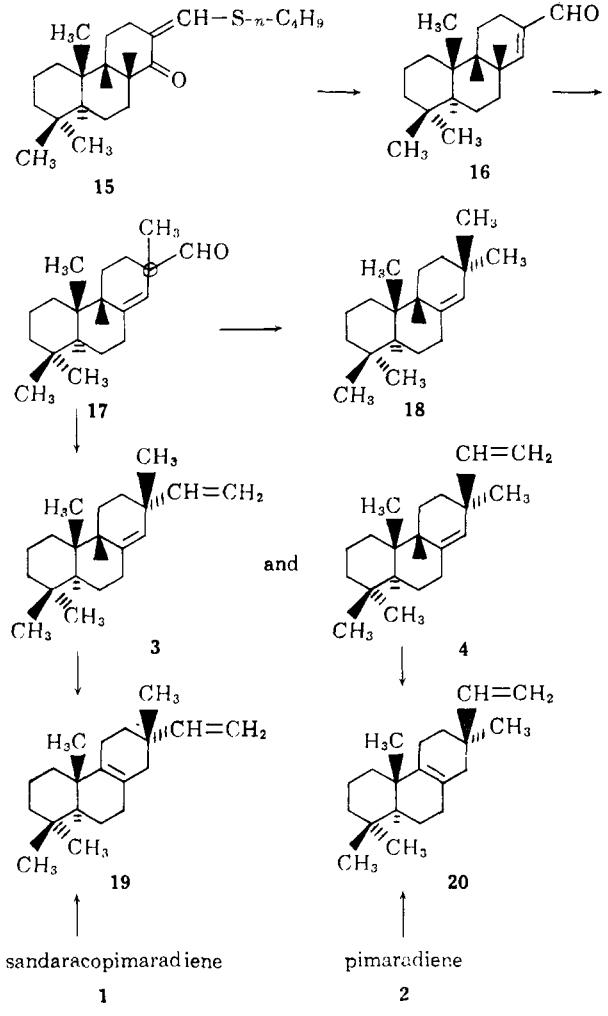
The aldehyde **7**, available from earlier work,[9] was converted to the allylic alcohol **8** in 77% yield through the agency of methyllithium. Equilibration[10] of this alcohol with excess ethyl vinyl ether afforded the vinyl ether **9** in 66% yield. We attribute the markedly lower



7 8 9 10 11 12 13 14

yield observed in the formation of the vinyl ether **9** as compared with the 91% yield observed in the formation of the ether **5** to the secondary *vs.* primary nature of the hydroxyl function. The vinyl ether **9** was also less stable than its homolog **5** and more susceptible to hydrolysis. However, pyrolysis[11] of the chromatographically pure material generated as high as a 97% yield of the corresponding aldehyde **10**. While the stereochemistry of the newly introduced acetaldehyde residue was surely known, the configuration of the ethylidene group was not determined, as this wou be of no consequence to the sequel. The aldehyde **10** was quite susceptible to air oxidation and was characterized as the corresponding acid (silver oxide oxidation[12]), its methyl ester, and the acetal **11**, prepared in 91% yield by acid catalyzed, azeotropic removal of water from a solution of the aldehyde and ethylene glycol in benzene. On hydroboration[13] the acetal **11** afforded an alcohol which was not purified but oxidized directly with Jones reagent[14] to the corresponding ketone. Chromatography of this oxidation mixture served not only to remove any impurities but also to equilibrate the C-8 acetyl residue through its enol and thus establish the α-(equatorial) orientation. In this manner we were able to realize a 60% over-all yield of the crystalline keto acetal **12**. Achievement of our first goal was readily accomplished by acid-catalyzed acetal hydrolysis and then acid-catalyzed aldol-type cyclization of the crude keto aldehyde. The tricyclic unsaturated ketone **13** formed in this way in 65% yield was reduced in 95% yield to its saturated analog **14** over 10% palladium on carbon. The alarm created by the observation that the melting point of this *trans-syn-cis* ketone **14** (78–79.5°) was the same as that of the isomeric *trans-anti-trans* ketone (78–80°) prepared earlier[4] was quieted when on admixture the melting point was dramatically depressed to 45–67°; the infrared spectra of the two ketones also showed significant differences in the 7–16-μ region.

The remaining steps of the synthesis closely paralleled the aldehyde method used earlier[4] for the construction



15 16 17 18 19 20 1 2

(10) W. H. Watenabe and L. E. Conlon, *J. Am. Chem. Soc.*, **79**, 2828 1957).

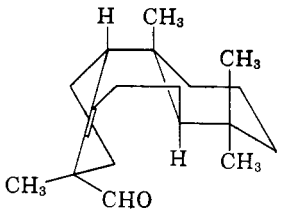
(11) A. W. Burgstahler and I. C. Nordin, *ibid.*, **83**, 198 (1961).

(12) K. J. Clark, G. I. Fray, R. H. Jaeger, and R. Robinson, *Tetrahedron*, **6**, 217 (1959).

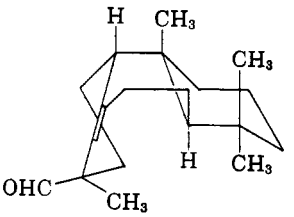
(13) H. C. Brown, K. J. Murray, L. J. Murray, J. A. Snover, and G. Zweifel, *J. Am. Chem. Soc.*, **82**, 4233 (1960).

(14) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946); see also, C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

of (±)-sandaracopimaradiene (**1**) and (±)-pimaradiene (**2**). Thus the ketone **14** was converted to the 13-*n*-butylthiomethylene derivative **15** by the standard procedure[15] in an average yield of 79%. Sodium borohydride reduction of this derivative **15**, and then steam distillation of the crude product from aqueous sulfuric acid[16] afforded a 70% over-all yield of the aldehyde **16**. It proved to be more difficult to effect enolization of the aldehyde **16** than its *trans-anti-trans* epimer,[4] for it was not until a solution of this aldehyde in benzene–*t*-butyl alcohol containing a 210-fold excess of potassium *t*-butoxide was refluxed for one-half hour that any appreciable coloration due to the enolate could be detected. Addition of methyl iodide to this mixture then effected the desired end and afforded an 81% yield of 13-methylated material **17**, together with 8% starting aldehyde and 11% of unidentified material, as measured by gas-liquid chromatography. The presence of two methylated aldehydes in approximately equal proportions was also determined by this technique. Unfortunately, these aldehydes were not as stable as those obtained in the *trans-anti-trans* series,[4] and on column chromatography over Florisil extensive decomposition occurred. We were able to isolate a small amount of the more strongly adsorbed aldehyde in a crystalline, analytically pure state, but its epimer could not be obtained in a pure condition. By virtue of this chromatographic behavior, we tentatively assigned the crystalline isomer the 13-α-methyl-13β-aldehydo structure **17b**. This assignment proved to be correct (*vide infra*) and pointed up the interesting effect of the conformation of the *trans-syn*-$\Delta^{8(14)}$-structure on the adsorption of these molecules. It can be seen from structures **17a** and **17b** that although the β-aldehydo grouping in isomer **17b** is quasi-axial, it is more exposed and thus more available for adsorption than the α-aldehyde in the quasi-equatorial position in the epimer **17a**. Such a reversal of the more common trend can be attributed to the *syn*-backbone which forces the β-ring to adopt the boat conformation.



17a



17b

Lacking a satisfactory method of preparatively separating the unstable aldehydes **17**, the synthesis was completed by treating the aldehyde mixture with methylenetriphenylphosphorane,[17] and thereby generating a mixture of the dienes **3** and **4** together with small quantities of impurities. It was found that this much more stable diene mixture was readily resolved by gas-liquid chromatography on a polyester column, and by application of this technique on a preparative scale we were able to isolate pure samples of the individual dienes A and B.

(15) R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1615 (1962).

(16) This procedure proved superior to the acid hydrolysis used in the previous work,[4] as it prevented the formation of any appreciable quantities of dithioacetal from the aldehyde and liberated *n*-butyl mercaptan in the presence of mineral acid.

(17) G. Wittig and V. Schöllkopf, *Ber.*, **87**, 1318 (1954).

The problem of discerning which of our pure diene samples A and B corresponded to which of the structures **3** and **4** was greatly facilitated by the availability of sandaracopimaradiene **1** and pimaradiene **2** of rigorously established structure from our earlier work.[4] Thus by application of the acid-catalyzed isomerization technique of Edwards,[5b] sandaracopimaradiene **1** was transformed into $\Delta^{8,9}$-sandaracopimaradiene (**19**)[18] and pimaradiene **2** to $\Delta^{8(9)}$-pimaradiene (**20**). In this manner the only difference between the two series—namely, the asymmetry at C-9—was removed. It was satisfying to find that a similar acid treatment of the diene A (eluted first on gas-liquid chromatography) led to $\Delta^{8(9)}$-sandaracopimaradiene (**19**) and thereby established the structure **3** for this diene. Similarly, the diene B (eluted second from the gas-liquid column) was rearranged to $\Delta^{8(9)}$-pimaradiene (**20**), and thus must possess the structure **4**. In confirmation of our tentative structural assignment to the crystalline methylated aldehyde **17b** mentioned above, we found that treatment of this aldehyde **17a** with methylenetriphenylphosphorane[17] led to a 96% yield of the diene **4**.

While these interrelationships conclusively establish the stereochemistry of the two dienes **3** and **4** at C-13, they represent strong but only circumstantial evidence for the $\Delta^{8(14)}$-position of the nuclear double bond. As will be evident below, this became an extremely important point, and in order to gain more evidence for this assignment, the mixture of aldehydes **17** was reduced to the olefin **18** in 91% yield by employing the Huang–Minlon modification[19] of the Wolff–Kishner reduction. The n.m.r. spectrum of this olefin showed a single, uncoupled signal at 5.30 τ for the vinyl hydrogen present and thereby verified the $\Delta^{8(14)}$-position for the double bond. As a check on the reliability of this method of analysis, the corresponding *trans-anti-trans* olefin was prepared in a similar fashion in 92% yield from the epimeric mixture of *trans-anti-trans* aldehydes obtained previously.[4] Again the n.m.r. spectrum showed the presence of only a single, uncoupled band due to the C-14 vinyl hydrogen at 5.13 τ. Thus these observations, taken together with the demonstrated *trans-syn-cis* stereochemistry of the ketone **14** and the interrelation of the dienes **3** and **4** with the previously synthesized[4] pimaradienes **1** and **2**, conclusively establish the structure and stereochemistry of the dienes **3** and **4** as shown.

There remained but to compare the properties of the synthetic dienes 3 and 4 with isopimaradiene[20] and rimuene.[7] In view of the analysis presented above, it was not surprising to find that both the infrared spectrum and relative mobility on gas-liquid chromatography (Table I) of rimuene were markedly different from

(18) When $\Delta^{8(9)}$-sandaracopimaradiene (**19**) was obtained from (−)-sandaracopimaradiene (−**1**) by this same procedure, it crystallized and was found to melt at 52–53° after recrystallization from methanol. The close correspondence between the melting point of this material and that (m.p. 51–52°) described by V. Galik, J. Kuthan, and F. Petrů [*Chem. Ind.* (London), 722 (1960)] for the compound obtained by desulfurization of the ethylenethioacetal of sandaracopimaral prompts us to suggest their identity. The substance obtained by Petrů and originally reported to be rimuene was later shown by these workers to be different from the natural product by a direct comparison of the two materials. It is reasonable to conclude that isomerization of the $\Delta^{8(14)}$ double bond to the more highly substituted $\Delta^{8(9)}$ position could have taken place on the surface of the Raney nickel catalyst used for the desulfurization.

(19) Huang-Minlon, *J. Am. Chem. Soc.*, **68**, 2487 (1946).

(20) Prepared from isopimaric acid in 48% over-all yield by the same sequence employed earlier[4] (see the Experimental).

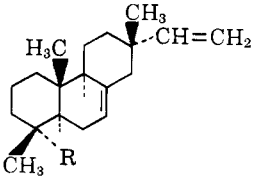
TABLE I
RELATIVE MOBILITY OF DIENES ON GAS-LIQUID CHROMATOGRAPHY

Rimuene	0.72	Pimaradiene	0.89
Diene **3**	0.74	Sandaracopimaradiene	1.00 (ref. std.)
Diene **4**	0.89	Isopimaradiene	1.23

those of the diene **4**. This result again struck down a proposed structure for rimuene and points up the need of more definitive chemical evidence before further structural assignments are made.

Quite surprising, however, was the lack of correspondence between the infrared spectrum and relative mobility on gas-liquid chromatography (Table I) between the synthetic diene **3** and isopimaradiene. Particularly striking were the differences in the 800–900-cm.$^{-1}$ region. The absorption in this region, which we have come to associate[4] with the gross hydrophenanthrene structure and stereochemistry, was quite simple in the spectrum of the synthetic diene **3** (ν_{max}^{film} 860 cm.$^{-1}$) and more complex in the spectrum of isopimaradiene and its derivatives (ν_{max}^{film} 820 cm.$^{-1}$, 835 cm.$^{-1}$ and 860 cm.$^{-1}$).

The non-identity of the synthetic diene **3** of known structure and stereochemistry with isopimaradiene occasioned a more thorough examination of the data available on the structure of the natural product. The evaluation of this evidence, together with some new results, are described in the following article[21] where it is shown that isopimaric acid—and thus isopimaradiene—possess the *trans-anti*-Δ^7-structures **21** and **22**, respectively.



21. R = —CO_2H
22. R = —CH_3

Experimental[22]

5,5,9β-Trimethyl-2-(1-hydroxyethyl)-*trans*-Δ¹-octalin (8).—To a well stirred solution of 0.16 mole of methyllithium in 200 ml. ether (prepared by bubbling methyl bromide into a cooled, stirred suspension of 2.2 g. (0.315 mole) of lithium in 200 ml. of ether) was added 22.5 g. (0.11 mole) of chromatographically pure 2-carboxaldehyde-5,5,9β-trimethyl-*trans*-Δ¹-octalin (**7**) in 50 ml. of ether, and the solution was stirred at room temperature for 8 hr. Saturated aqueous ammonium chloride (100 ml.) was added, and the product isolated by ether extraction in the usual manner. Evaporation of the ether and distillation of the residue afforded 18.60 gm. (77%) of the allylic alcohol **8**, b.p. 105–106° (0.3 mm.). The analytical sample, obtained by redistillation, boiled at 92° (0.15 mm.).

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.89; H, 11.75.

Infrared: λ_{max}^{film} 2.90 μ (s) (O—H); 9.39 μ (s) (C—O).

Vinyl Ether of 5,5,9β-trimethyl-2-(1-hydroxyethyl)-*trans*-Δ¹-octalin (9).—In a typical run, 3.75 g. (17.0 mmoles) of 5,5,9β-trimethyl-2-(hydroxyethyl)-*trans*-Δ¹-octalin (**8**) was dissolved in 40 ml. of freshly distilled ethyl vinyl ether containing 540 mg. of mercuric acetate. After the solution had been refluxed in a nitrogen atmosphere for 6 hr., 1 g. of anhydrous sodium carbonate was added, and the mixture was stirred 0.5 hr. The ethereal solution was decanted, the solid sodium carbonate was washed well with ether, and the combined ethereal fractions were evaporated on the steam bath under a stream of nitrogen. Chromatography of the residue on 130 g. of alumina afforded 2.790 g. (66%) of the vinyl ether (eluted with 3 l. of petroleum ether) which was of sufficient purity for use in the Claisen rearrangement. The vinyl ether **9** was characterized by its infrared spectrum [λ_{max}^{film} 3.12 μ (w) (vinyl H); 6.10 μ (s) and 6.20 μ (s) (vinyl ether)], but due to its sensitivity to atmospheric moisture. no satisfactory analytical values could be obtained.

5,5,9β-Trimethyl-2-ethylidene-*trans*-decal-1α-ylacetaldehyde (10).—A Carius tube containing 1.035 g. (4.2 mmoles) of the vinyl ether **9** under nitrogen was placed in an oil bath at 195°, and the temperature was maintained between 190–200° for 3 hr. The tube was cooled and the aldehyde was chromatographed on 100 g. of Florisil. After elution with 500 ml. of petroleum ether removed 30 mg. of oil, 1500 ml. of 3% ether:petroleum ether eluted 1.003 g. (97%) of the aldehyde **10**. In several runs it was found that the crude aldehyde before chromatography was of sufficient purity for acetalization without further purification. In four runs in which the aldehyde was purified by chromatography, the yields ranged from 89–97%.

Infrared: λ_{max}^{film} 3.67 μ (*CH*O); 5.80 μ (s) (>C=O); 6.00 μ and 12.15 μ) (>C=CH—CH_3).

5,5,9β-Trimethyl-2-ethylidene-*trans*-decal-1α-ylacetic Acid.—To a solution of 946 mg. of the aldehyde **10**, containing some allylic alcohol **8** in 50 ml. of ethanol containing 1.00 g. of silver nitrate and 10 ml. of water was added over a period of 1 hr. with rapid stirring a solution of 0.95 g. of sodium hydroxide in 35 ml. of water. The mixture was stirred for 4 hr. at room temperature, diluted with 50 ml. of water, and filtered. The clear filtrate was extracted three times with 40-ml. portions of ether (evaporation of the combined ether extracts afforded 400 mg. of recovered allylic alcohol **10**, identified by its infrared spectrum), acidified with excess concentrated hydrochloric acid, and the precipitated acid isolated by ether extraction. After the usual washing and drying procedure, removal of the ether and crystallization of the solid residue from ethyl acetate:petroleum ether afforded 545 mg. of the acid, m.p. 150–151°. The analytical sample, obtained after one further crystallization from the same solvent pair, also melted at 150–151°.

Anal. Calcd. for $C_{17}H_{28}O_2$: C, 77.22; H, 10.68. Found: C, 77.19; H, 10.53.

The **methyl ester**, prepared in 80% yield by the action of ethereal diazomethane on the acid, was a liquid which was evaporatively distilled at 90° (bath temp.) (0.1 mm.) for analysis.

Anal. Calcd. for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C. 77.43; H, 10.73.

Infrared: λ_{max}^{film} 5.78 μ (s) (>C=O) and 8.71 μ (s) (C—O—C).

Acetal of 5,5,9β-Trimethyl-2-ethylidene-*trans*-decal-1α-ylacetaldehyde (11).—A solution of 1.003 g. (4.04 mmoles) of the aldehyde **10**, 1 ml. of ethylene glycol, and 30 mg. of *p*-toluenesulfonic acid in 40 ml. of benzene was heated under reflux for 40 min. using a Dean–Stark water separator filled with Drierite to remove water from the distillate. After the usual work-up and removal of the solvent, the residue was chromatographed on 45 g. of alumina. Elution with 2.5% ether:petroleum ether afforded 1.079 g. (91%) of the acetal **11** of sufficient purity to be used directly in the hydroboration experiment to follow. The analytical sample was obtained by evaporative distllation at 110° [bath temp. (0.2 mm.)].

Anal. Calcd. for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 77.97; H, 11.12.

Infrared: λ_{max}^{film} 8.82 μ (s) (acetal); 6.00 μ and 12.20 μ (>C=CHCH$_3$).

Acetal of 5,5,9β-Trimethyl-2α-acetyl-*trans*-decal-1α-ylacetaldehyde (12).—To 25.0 ml. of a 0.083 *M* solution of diborane in dry tetrahydrofuran (prepared by the addition of boron trifluoride–ethereate to a suspension of sodium borohydride in tetrahydrofuran, filtration, and gasometric standardization) in a

(21) See also, R. E. Ireland, and J. Newbould, *J. Org. Chem.*, **27**, 1931 (1962), and W. Antkowiak, J. W. ApSimon, and O. E. Edwards, *J. Org. Chem.*, **27**, 1930 (1962), for preliminary reports of these results.

(22) Unless specified otherwise, the term "petroleum ether" refers to reagent grade material boiling in the range 30–60°. All gas–liquid chromatograms were obtained on a Barber–Coleman Model 10 gas-liquid chromatography unit using a 6-ft. column packed with 15% diethylene glycol succinate on Chromosorb W. Melting points were determined on a Kofler Hot Stage and are corrected for stem exposure. Analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. Unless otherwise specified infrared spectra were measured on a Perkin–Elmer Infracord Model 137, and strong bands are marked (s); all others reported are of moderate intensity unless otherwise specified. Ultraviolet spectra were determined on a Cary recording spectrophotometer (Model 11 MS). *Florisil* refers to the product of the Floridin Company, Tallahassee, Fla., 60/100 mesh.

nitrogen atmosphere was added with stirring a solution of 1.00 g. (3.4 mmoles) of the acetal olefin **11** in 8 ml. of tetrahydrofuran. Stirring was continued for 2 hr. at room temperature, and then 5 ml. of 10% aqueous sodium hydroxide was added followed by 5 ml. of 30% hydrogen peroxide. After the reaction mixture was heated under reflux for 1 hr., 100 ml. of water was added, and the product isolated in the usual manner by ether extraction. The residue obtained after removal of the ether was not further purified but dissolved in 20 ml. of acetone, cooled to 0°, and oxidized with 0.90 ml. (7.1 meq.) of Jones reagent.[14] After the addition of 100 ml. of cold water, the product was isolated by ether extraction in the usual manner. The oily residue, obtained after removal of the ether, was chromatographed on 40 g. of alumina. Elution with 1200 ml. of 1% ether:benzene afforded 870 mg. of crystalline keto acetal **12**. After one crystallization of this material from petroleum ether (b.p. 60–75°), there remained 633 mg. (60%) of material, m.p. 126–130°, of sufficient purity to be used in further experiments. The analytical sample, obtained by further crystallization from the same solvent, melted at 132–133.5°.

Anal. Calcd. for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. Found: C, 73.83; H, 10.57.

Infrared: $\lambda_{max}^{HCCl_3}$ 5.87 μ (s) (>C=O); 8.82 μ (s) (acetal).

(±)-9-Isopodocarpen-12-one-14 (13).—To a solution of 6.70 g. (21.6 mmoles) of the keto acetal **12** in 80 ml. of acetone was added 20 ml. of 10% aqueous hydrochloric acid, and the reaction mixture was allowed to stand 2 hr. at room temperature. The solution was then diluted with 30 ml. of saturated aqueous sodium chloride, and the product isolated in the customary fashion by ether extraction. A solution of the crude keto aldehyde, obtained by removal of the ether and not further purified, in 100 ml. of benzene containing 100 mg. of *p*-toluenesulfonic acid was heated under reflux in a nitrogen atmosphere for 1.5 hr. After the usual work-up, removal of the solvent left a crystalline solid which was chromatographed on 200 g. of alumina. Elution with 4 l. of benzene afforded 4.6 g. of the ketone **13**. After crystallization of this material from petroleum ether (b.p. 60–75°), there remained 3.50 g. (65%) of material melting at 113–115°. The analytical sample, obtained by one more crystallization from the same solvent, melted at 116–117°.

Anal. Calcd. for $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 82.75; H, 10.44.

Ultraviolet: λ_{max}^{alc} 227 mμ (ϵ 8700). **Infrared:** $\lambda_{max}^{HCCl_3}$ 6.01 μ (s) (α,β-unsaturated >C=O).

(±)-9-Isopodocarpanone-14 (14).—A solution of 500 mg. (2.03 mmoles) of the ketone **13** in 10 ml. of glacial acetic acid in which was suspended 50 mg. of 10% palladium-on-carbon was stirred in a hydrogen atmosphere at room temperature for 3 hr., during which time 51.3 ml. (100%) of hydrogen was absorbed. After removal of the catalyst by filtration, most of the acetic acid was removed at reduced pressure, and the residue was treated with water and ether. The ethereal solution was separated, washed, and dried in the usual manner and evaporated at reduced pressure. On crystallization of the residue from petroleum ether (b.p. 60–75°) there was obtained 475 mg. (95%) of the ketone **14**, m.p. 78–79.5°, in an analytically pure condition.

Anal. Calcd. for $C_{17}H_{28}O$: C, 82.20; H, 11.36. Found: C, 82.28; H, 11.38.

Infrared: $\lambda_{max}^{HCCl_3}$ 5.91 μ (saturated (s) >C=O).

The melting range of a mixture of this ketone and the isomeric *trans-anti-trans* ketone,[4] m.p. 78–80°, was depressed to 45–67°.

(±)-13-*n*-Butylthiomethylene-9-isopodocarpanone-14 (15).—Hydroxymethylation of 569 mg. (2.3 mmoles) of the ketone **14** was accomplished according to the standard procedure by employing 6.0 g. (0.12 mole) of sodium methoxide and 10 ml. (0.12 mole) of ethyl formate in 20 ml. of benzene. The crude derivative, obtained in essentially quantitative yield, in 15 ml. of benzene containing 0.025 ml. of *n*-butyl mercaptan and 10 mg. of *p*-toluenesulfonic acid was heated under reflux in a nitrogen atmosphere for 4 hr. After the customary work-up, there was obtained 629 mg. (79%) of the crystalline thiomethylene derivative (**15**), m.p. 70–73°. The analytical sample, obtained by crystallization of this derivative from petroleum ether (b.p. 60–75°), melted at 73–74°.

Anal. Calcd. for $C_{22}H_{36}OS$: C, 75.81; H, 10.41; S, 9.19. Found: C, 75.83; H, 10.30; S, 9.32.

Infrared: λ_{max}^{film} 6.01 μ (s) (conj. >C=O); 6.48 μ (s) (conj. >C=C<).

(±)-9-Isopodocarp-13-ene-13-carboxaldehyde (16).—A solution of 600 mg. (1.7 mmoles) of the thiomethylene derivative **15** in 30 ml. of methanol was reduced with a solution of 1.0 g. (26 mmoles) of sodium borohydride in 8 ml. of 0.1 *N* aqueous sodium hydroxide. After stirring for 2 hr. at room temperature, most of the methanol was removed at reduced pressure, and the product isolated by ether extraction. The crude reduction product was washed into a solution of 200 ml. of diethylene glycol and 100 ml. of 10% aqueous sulfuric acid by using a small quantity of ether, and the acidic mixture subjected to steam distillation. Ether extraction of 4 l. of steam distillate and chromatography of the solute on 30 g. of alumina afforded 408 mg. of crystalline material, eluted with 500 ml. of 50% benzene:petroleum ether. Crystallization of this solid from petroleum ether (b.p. 60–75°) gave 312 mg. (70%) of the aldehyde **16**, m.p. 107.5–109°, in an analytically pure condition.

Anal. Calcd. for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 83.08; H, 10.91.

Infrared: $\lambda_{max}^{HCCl_3}$ 3.64 μ (w) (C*H*O); 5.96 μ (s) (conj. >C=O); 6.08 μ (conj. >C=C<).

(±)-13-Methyl-9-isopodocarp-8(14)-ene-13-carboxaldehyde (17).—A solution of 416 mg. (1.44 mmoles) of the aldehyde **16** in 15 ml. of benzene was added to a slush prepared from 12 g. (0.3 mole) of potassium in 240 ml. of *t*-butyl alcohol contained in a nitrogen atmosphere. After stirring and heating this reaction mixture under reflux for 0.5 hr., the suspension was cooled in an ice bath for 4 min., and then 40 ml. (86 g.; 0.6 mole) of methyl iodide was added all at once. The mixture was stirred for 8 hr. at room temperature; 100 ml. of water was added and most of the *t*-butyl alcohol removed at reduced pressure. The product was isolated by ether extraction in the usual manner and evaporatively distilled at 140–145° (bath temp.) (0.02 mm.). In this manner there was collected 422 mg. of colorless distillate which on gas-liquid chromatography was shown to be comprised of 36% methylated aldehyde isomer A **17a**, 40% of isomer B **17b** [together representing 81% of methylated aldehyde **17**], 8% of starting aldehyde **16**, and 16% of less mobile, unidentified impurity. Infrared spectral analysis showed the presence of both a saturated aldehyde (band at 5.78 μ) and conjuated unsaturated aldehyde (weaker band at 5.91 μ).

Chromatography of 255 mg. of a similar distilled mixture on 25 g. of Florisil led to extensive decomposition and recovery of only 80% of the material. Besides several oily early fractions, there was obtained 88 mg. of a crystalline sample of isomer B **17b** (identified by relative mobility on gas-liquid chromatography) eluted with 1200 ml. of 10% benzene:petroleum ether, and 21 mg. of the aldehyde **16** (identified by comparison of infrared spectra) eluted with 300 ml. of benzene. After two crystallizations of the aldehyde isomer B **17b** from petroleum ether at −78°, there was obtained a 26-mg. sample melting at 82–87° and shown to be 99% pure by gas-liquid chromatography.

Anal. Calcd. for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.13; H, 11.19.

(±)-9-Isopimaradiene (4) and (±)-9-Iso-sandaracopimaradene (3).—The distilled mixture of aldehydes **17** described above (422 mg.) was dissolved in 10 ml. of dry ether and added under nitrogen to a stirred suspension of 3.18 g. (9.0 mmoles) of triphenylmethylphosphonium bromide and 930 mg. (8.3 mmoles) of powdered potassium *t*-butoxide in 80 ml. of petroleum ether. The mixture was stirred for 10 hr. at room temperature, 30 ml. of water added, and the organic layer separated and dried (Na_2SO_4). The residue obtained after filtration and evaporation of the solvent was chromatographed on 20 g. of alumina. Elution with 100 ml. of petroleum ether afforded a mixture of dienes A **3** (49%) and B **4** (46%) together with 5% of what was probably the conjugated diene from the aldehyde **16** (percentages obtained by gas-liquid chromatography).

This mixture of dienes was separated by gas-liquid chromatography on a column 9 ft. long and 0.5 in. in outside diameter, packed with a stationary phase of 15.3% ethylene glycol–succinic acid polyester on Chromosorb W support. This column was found to have *ca.* 600 theoretical plates. Using the Barber–Coleman Model 10 apparatus, a column temperature of 200° and argon pressure of 16 p.s.i., the dienes A **3** and B **4** were eluted at 13 and 16 min., respectively. Collection was accomplished by passing the effluent gases alternately through each of two short, 8-mm. i.d. tubes packed with a small plug (*ca.* 0.5–1 gm.) of alumina, from which the individual dienes could be readily eluted with petroleum ether. Employing 5-μl. samples, a total of 145 μl. of the diene mixture afforded 29 mg. of diene A **3** and 34 mg. of diene B **4**. Each diene was individually evaporatively distilled at 100–110° (bath temp.) (0.2 mm.) and analyzed

by gas-liquid chromatography. Diene A **3** was found to be 98% pure (2% of diene B) with a mobility relative to (−)-sandaracopimaradiene (−1) of 0.74 and diene B **4** was found to be 99% pure (1% of diene A) with a mobility relative to the same reference standard of 0.89.

Anal. Calcd. for $C_{20}H_{32}$: C, 88.16; H, 11.84. Found for diene A **3**: C, 88.08; H, 11.76. Found for diene B **4**: C, 87.93; H, 11.76.

Infrared[23]: **Diene A (3).**—ν_{max}^{film} 3080 cm.$^{-1}$ (w) (vinyl H); 1835 cm.$^{-1}$ (w), 1639 cm.$^{-1}$, 995 cm.$^{-1}$, and 918 cm.$^{-1}$ (—CH=CH_2); 1662 cm.$^{-1}$ (w) and 819 cm.$^{-1}$ (w) (trisubst. >C=C<); 860 cm.$^{-1}$ (skeletal vibration).

Diene B. (4).—ν_{max}^{film} 3080 cm.$^{-1}$ (w) (vinyl H); 1820 cm.$^{-1}$ (w), 1635 cm.$^{-1}$, 997 cm.$^{-1}$ and 910 cm.$^{-1}$ (—CH=CH_2); 1660 cm.$^{-1}$ (w) and 818 cm.$^{-1}$ (w) (trisubst. >C=C<); 861 cm.$^{-1}$ (skeletal vibration).

When 22 mg. (0.08 mmole) of the aldehyde isomer B (**17b**) was treated as above with 1.09 gm. (3.0 mmoles) of triphenylmethylphosphonium bromide and 310 mg. (2.8 mmoles) of powdered potassium *t*-butoxide in 20 ml. of petroleum ether, there resulted 21 mg. (96%) of the corresponding diene after chromatographic purification over alumina. The infrared spectrum and relative mobility on gas-liquid chromatography of the diene prepared in this manner were identical to those of the diene B **4** obtained from the mixture above.

8(9)-Sandaracopimaradiene (19): From (−)-Sandaracopimaradiene (−1).—A solution of 40 mg. of (−)-sandaracopimaradiene, (−1) m.p. 41–42°, in 10 ml. of dry chloroform was cooled in an ice–salt bath and treated with a stream of dry hydrogen chloride for 4 hr. The solution was diluted with 40 ml. of petroleum ether, washed with two 15-ml. portions of water, one 15-ml. portion of 10% aqueous sodium bicarbonate, and dried (Na_2SO_4). After filtration and removal of the solvent, the residue was eluted from 5 g. of alumina with 20 ml. of petroleum ether and then evaporatively distilled at 100–110° (bath temp.) (0.2 mm.). In this manner there was obtained 38 mg. (95%) of 8(9)-sandaracopimaradiene (**19**), m.p. 45–50°. The analytical sample, obtained after two crystallizations from methanol, melted at 52–53°.

Anal. Calcd. for $C_{20}H_{32}$: C, 88.16; H, 11.84. Found: C, 88.12; H, 11.92.

Infrared[23]: ν_{max}^{film} 3080 cm.$^{-1}$ (w) (vinyl H); 1822 cm.$^{-1}$ (w), 1640 cm.$^{-1}$, 995 cm.$^{-1}$, and 910 cm.$^{-1}$ (—CH=CH_2).

From Diene A (3).—Treatment of 23 mg. of the diene A **3** (98% pure by gas-liquid chromatography) in the same manner led to the production of 22 mg. (96%) of (±)-8(9)-sandaracopimaradiene (**19**), as an oil. Gas-liquid chromatography indicated the presence of a single substance, the relative mobility of which was identical to the material obtained above from the natural diene. The infrared spectra of the natural and synthetic dienes were identical.

8(9)-Pimaradiene (20). From (+)-Pimaradiene.—When 38 mg. of (+)-pimaradiene (**4**) was rearranged by treatment with dry hydrogen chloride in 10 ml. of dry chloroform in exactly the same manner as described above, there resulted 37 mg. (96%) of the 8(9)-pimaradiene (**20**), as an oil. The analytical sample was obtained by evaporative distillation at 100–110° (bath temp.) (0.2 mm.). Gas-liquid chromatography of this material showed the presence of a single component to the extent of 99%.

Anal. Calcd. for $C_{20}H_{32}$: C, 88.16; H, 11.84. Found: C, 88.05; H, 11.75.

Infrared[23]: ν_{max}^{film} 3080 cm.$^{-1}$ (w) (vinyl H); 1820 cm.$^{-1}$ (w), 1638 cm.$^{-1}$, 995 cm.$^{-1}$, and 908 cm.$^{-1}$—CH=CH_2).

From Diene B (4): When 42 mg. of the diene B **4** (99% pure by gas-liquid chromatography) in 10 ml. of dry chloroform was rearranged with dry hydrogen chloride as described above, there resulted 41 mg. (96%) of (±)-8(9)-pimaradiene (**20**), as an oil. Gas-liquid chromatography indicated the presence of a single substance, the relative mobility of which was identical to the material obtained above from the natural diene. The infrared spectra of the natural and synthetic dienes were identical.

(±)-13,13-Dimethyl-9-isopodocarp-8(14)-ene (18).—A solution of 180 mg. (0.66 mmole) of the distilled mixture of aldehydes **17** and 1 ml. of 98–100% hydrazine hydrate in 16 ml. of diethylene glycol was heated in a nitrogen atmosphere at 100° for 30 min. and then at 140° for 30 min. Then 1.26 g. of potassium hydroxide was added, and the temperature raised to 210° and held there for 3 hr. The reaction mixture was cooled, diluted with water, and the product isolated with petroleum ether in the usual fashion. Chromatography of the residue, obtained after removal of the solvent, on 5 g. of alumina affords 161 mg. of oil, eluted with 30 ml. of petroleum ether. After evaporative distillation of this material at 110° (bath temp.) (0.2 mm.), there remained 156 mg. (91%) of the olefin **18**. Gas-liquid chromatography of this material showed the presence of one component to the extent of 94%.

Anal. Calcd. for $C_{19}H_{32}$: C, 87.61; H, 12.39. Found: C, 87.51; H, 12.43.

Infrared: λ_{max}^{film} 11.61 μ (skeletal vibration).

N.m.r.[24]: 5.30 τ (3.0 c.p.s. 1/2 band width) (vinyl H); 9.00 τ, 9.14 τ (area double other signals), 9.16 τ, and 9.21 τ (five quaternary methyl groups).

(±)-13,13-Dimethylpodocarp-8(14)-ene.—In the same fashion as described above for its 9β-epimer (**17**) 418 mg. (1.53 mmoles) of an epimeric mixture of 13-methylpodocarp-8(14)-en-13-carboxaldehyde[4] was reduced in 16 ml. of diethylene glycol with 1 ml. of 98–100% hydrazine hydrate and 1.26 g. of potassium hydroxide. After the same work-up, chromatography and distillation procedure, there resulted 358 mg. (90%) of the olefin as an oil. This material was shown to consist of a single component to the extent of 96% by gas-liquid chromatography.

Anal. Calcd. for $C_{19}H_{32}$: C, 87.61; H, 12.39. Found: C, 87.48; H, 12.41.

Infrared: λ_{max}^{film} 11.55 μ and 11.71 μ (skeletal vibrations).

N.m.r.[24]: 5.13 τ (3.0 c.p.s. 1/2 band width) (vinyl H); 8.92 τ, 9.15 τ (area triple other signals) and 9.30 τ (five quaternary methyl groups).

(−)-Isopimaradiene.—Reduction of 470 mg. (1.5 mmoles) of methyl isopimarate,[5a] m.p. 61–63°, with lithium aluminum hydride in ethereal solution in the customary manner afforded 430 mg. (99%) of isopimarol, as an oil. The analytical sample was obtained by evaporative distillation at 135° (bath temp.) (0.02 mm.).

Anal. Calcd. for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.10; H, 11.03.

Infrared: λ_{max}^{film} 2.91 μ (O—H); 3.20 μ (w) (vinyl H); 5.48 μ (w), 6.08 μ, 10.00 μ, and 10.98 μ (s) (—CH=CH_2); 11.62 μ, 11.98 μ, and 12.20 μ (skeletal vibrations).

When 425 mg. (1.5 mmoles) of isopimarol was oxidized with 0.36 ml. of Jones reagent[14] in 25 ml. of acetone, there resulted 425 mg. of crude isopimaral, as an oil, after the usual work-up.[4]

Infrared: λ_{max}^{film} 3.68 μ (s) (—C*H*O); 5.80 μ (s) (>C=O); together with all the vinyl and skeletal bands recorded above.

This crude isopimaral was not further purified but converted directly to the semicarbazone by treatment of a methanol solution with 0.80 ml. of a standard[25] aqueous solution of semicarbazine hydrochloride and 13 drops of pyridine. In this fashion there was obtained 270 mg. (53%) of isopimaral semicarbazone, m.p. 219–221°, after two crystallizations from methanol.

Anal. Calcd. for $C_{21}H_{33}N_3O$: C, 73.42; H, 9.68. Found: C, 73.58; H, 9.76.

When 220 mg. (0.64 mmole) of this semicarbazone was reduced, according to the procedure described earlier,[4] in 8 ml. of diethylene glycol with 2.6 g. of potassium hydroxide, there resulted 154 mg. (90%) of isopimaradiene $[\alpha]^{25}D$ −28° (*c*, 208 mg./100 ml., $CHCl_3$) in an analytically pure condition after chromatography on alumina and evaporative distillation at 90° (bath temp.) (0.05 mm.). This material was entirely homogeneous by gas-liquid chromatography and had a mobility relative to (−)-sandaracopimaradiene (−1) of 1.23. Neither this relative mobility nor the infrared spectrum of isopimaradiene were the same as the diene **3**.

Anal. Calcd. for $C_{20}H_{32}$: C, 88.16; H, 11.84. Found: C, 88.25; H, 11.69.

Infrared[23]: ν_{max}^{film} 3080 cm.$^{-1}$ (w) (vinyl H); 1821 cm.$^{-1}$ (w), 1639 cm.$^{-1}$, 995 cm.$^{-1}$, and 910 cm.$^{-1}$ (—CH=CH_2); 1669 cm.$^{-1}$ (w) (trisubst. >C=C<); 860 cm.$^{-1}$, 835 cm.$^{-1}$ and 820 cm.$^{-1}$ (skeletal vibrations).

Acknowledgment.—The authors greatly appreciate the assistance given them by Dr. O. E. Edwards of the National Research Council (Canada) in providing

(23) Determined on a Beckman IR-7 instrument through the courtesy of the Parke-Davis and Company spectrographic Laboratory.

(24) Measured at 60 Mc. in deuteriochloroform related to tetramethylsilane as an internal standard on a Varian Associates HR-60 spectrometer.

(25) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, Mass., 1955, p. 85.

generous supplies of the resin acids. Grateful appreciation is also due to Professor M. T. Rogers of Michigan State University as well as Dr. Edwards for the n.m.r. spectra. We are grateful to Professor L. H. Briggs of the University of Auckland (New Zealand) for providing a sample of rimuene.

Experiments Directed toward the Total Synthesis of Terpenes. VI. The Stereochemistry of Isopimaric Acid[1,2]

ROBERT E. IRELAND AND JOHN NEWBOULD

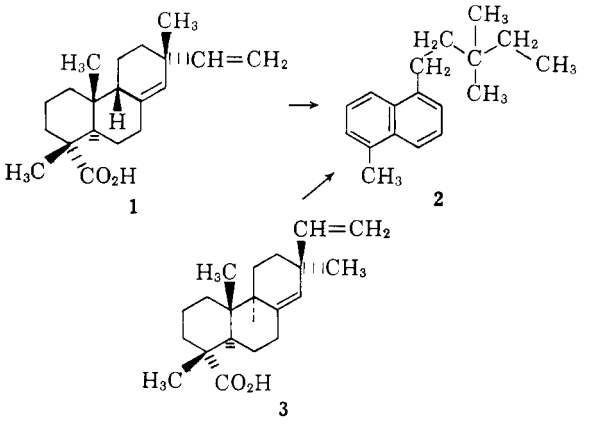
Department of Chemistry, The University of Michigan, Ann Arbor, Michigan

Received August 14, 1962

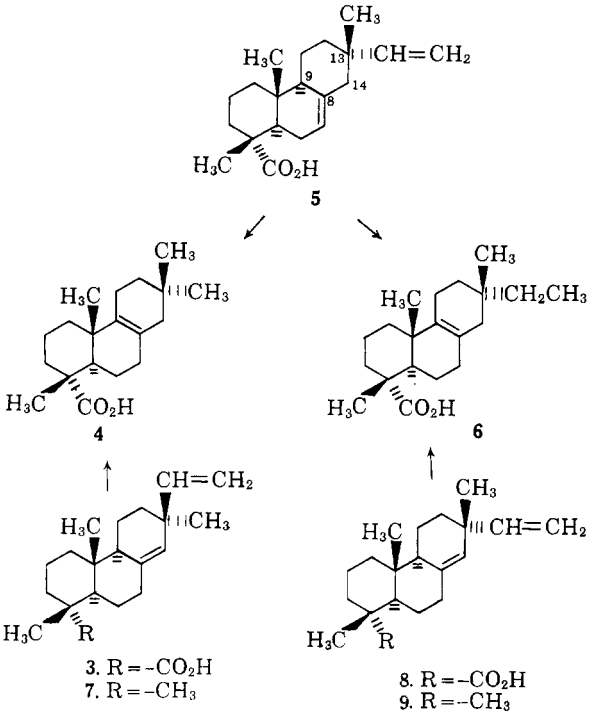
The stereochemistry of isopimaric acid (**5**) is elucidated by conversion to 13,13-dimethylpodocarpane (**16**), and comparison of this hydrocarbon with its racemate (**22**).

The synthesis of the epimeric (±)-9-isopimaradienes[3] conclusively showed that the long accepted structure 1 for isopimaric acid was incorrect, when neither diene was found identical with isopimaradiene. Needless to say, this result occasioned careful scrutiny of the properties of this acid and its corresponding diene to determine where the discrepancy lay.

In the initial investigation of the structure of isopimaric acid in 1948, Harris and Sanderson[4a] suggested that the resin acid had the pimaric acid carbon skeleton, and it was as a result of their degradation of both isopimaric (**1**) and pimaric (**3**) acid to the same naphthalenoid hydrocarbon (**2**) that they placed the nuclear double bond of both acids in the 8(14)-position. This proof of the position of this double bond has been accepted by all subsequent workers, in spite of some of the contortions to which they had to resort in order to rationalize their results. While such an interrelation would appear substantial enough, the reaction sequence used involved several reactions, such as ozonization and palladium-catalyzed dehydrogenation, during which skeletal rearrangements and redistributions might have occurred. Application of the more modern methods together with spectral interpretations seems advisable.



The well executed and extensive studies of Edwards and his collaborators[4b,c] have served to establish more rigorously that isopimaric (**5**) and pimaric (**3**) acids have the same carbon skeleton. Thus, both acids were converted to the same $\Delta^{8(9)}$-19-norpimaric acid (**4**).[4c] While this transformation establishes the identity of the carbon skeletons of the two acids, it implies nothing concerning their relative stereochemistry at C-9 and C-13 nor the location of the nuclear double bond.



Correlation[5] of isopimaric (**5**) and sandaracopimaric (**8**) acids through the identity of the $\Delta^{8(9)}$-dihydrosandaracopimaric acid (**6**) obtained from both acids meant that isopimaric acid (**5**) must differ from sandaracopimaric acid (**8**) only in the stereochemistry at C-9 and/or the location of the nuclear double bond. The latter possibility was not considered at the time.

Several investigations[4b-m,5] have been made of the stereochemistry at C–13 of the pimaric acids. While all

(1) For a preliminary report of this work, see R. E. Ireland and J. Newbould, *J. Org. Chem.*, **27**, 1930 (1962).

(2) This work was made possible through a grant from the National Science Foundation (G-19481).

(3) R. F. Church and R. E. Ireland, *J. Org. Chem.*, **28**, 17 (1963).

(4) (a) G. C. Harris and T. F. Sanderson, *J. Am. Chem. Soc.*, **70**, 2081 (1948); (b) O. E. Edwards and R. Howe, *Can. J. Chem.*, **37**, 760 (1959); (c) O. E. Edwards and R. Howe, *Chem. Ind.* (London), 537 (1959); (d) E. Wenkert and J. W. Chamberlin, *J. Am. Chem. Soc.*, **81**, 688 (1959); (e) B. Green, A. Harris, and W. B. Whalley, *J. Chem. Soc.*, 4715 (1958); (f) A. K. Bose, *Chem. Ind.* (London), 1105 (1960); (g) H. H. Bruun, *Acta Acad. Aboensis, Math. Phys.*, **19** (3), 7 (1954); (h) H. H. Bruun, *Finska Kemistsam-Fredets Medd.*, **63**, 22 (1945); (i) H. H. Bruun, *Acta. Chem. Scand.*, **6**, 798 (1952); (j) H.H. Bruun, I. Fishmeister, and E. Stenhagen, *ibid.* **13**, 379 (1959); (k) H. H. Bruun, R. Ryage, and E. Stenhagen, *ibid.*, **12**, 789 (1958); (l) Le-van-Thoi and J. Ourgand, *Bull. soc. chim. France*, 202 (1956); (m) G. W. A. Milne and H. Smith, *Chem. Ind.* (London), 1307 (1961).

(5) O. E. Edwards, A. Nicolson, and M. N. Rodger, *Can. J. Chem.*, **38**, 663 (1960).