

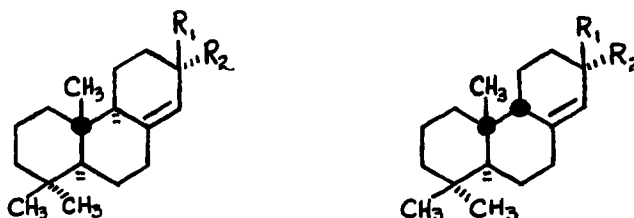
THE SYNTHESIS OF THE dl-9-iso-PIMARADIENES AND THE
REVISION OF THE STRUCTURES OF ISOPIMARIC ACID
AND RIMUENE

Robert F. Church¹ and Robert E. Ireland

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

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THE recently recorded² synthesis of dl-sandaracopimaradiene (1) and dl-pimaradiene (2) from this laboratory



(1) R₁ = -CH₃; R₂ = -CH=CH₂

(2) R₁ = -CH=CH₂; R₂ = -CH₃

(3) R₁ = -CH₃; R₂ = -CH=CH₂

(4) R₁ = -CH=CH₂; R₂ = -CH₃

established the stereochemistry of the corresponding resin acids, and showed that the structure first suggested³ for the diterpenoid hydrocarbon rimuene - namely, sandaracopimaradiene (1) - was incorrect⁴. As a continuation of our

¹ Sun Oil Company Fellow, 1959-1960.

² R. E. Ireland and P. W. Schiess, Tetrahedron Letters No. 25, 37 (1960).

³ L. H. Briggs, B. F. Cain, B. R. Davis and J. K. Wilmhurst, Tetrahedron Letters No. 8, 13 (1959); L. H. Briggs, B. F. Cain and J. K. Wilmhurst, Chemistry and Industry 599 (1958).

⁴ The previously (V. Galik, J. Kuthan and F. Petrú, Chemistry and Industry 722 (1960)), claimed conversion of sandaracopimaric acid to rimuene has been found to be in error (private communication from F. Petrú).

interest in methods of constructing the ring C substitution pattern of the pimaric acids, we have undertaken the synthesis of the 9-iso-pimaradienes (3) and (4), having the trans-syn-phenanthrene backbone. Interest in these structures was heightened recently by a preliminary report by Wenkert and Beak⁵ "confirming" that rimuene was represented by the structure (4). A necessary assumption for this assignment was that isopimaradiene have the stereochemistry depicted in structure (3). We wish to report here the successful synthesis of the 9-iso-pimaradienes (3) and (4) and show that neither structure corresponds to rimuene or isopimaradiene.

Treatment of the unsaturated aldehyde (5)⁶ with methyl lithium afforded an 85% yield of the alcohol (6), b.p. 105-106°/0.3 mm. (C, 80.89%; H, 11.75%). Equilibration⁷ of this alcohol with ethyl vinyl ether and pyrolysis⁸ of the resulting vinyl ether afforded an aldehyde⁹ (acid (Ag₂O), m.p. 150-151°, C, 77.19%; H, 10.53%) which was protected as the acetal (7), b.p. 110°/0.2 mm. (C, 77.97%; H, 11.12%) in an overall yield 53%. On hydroboration¹⁰ and oxidation

⁵ E. Wenkert and P. Beak, J. Amer. Chem. Soc. 83, 998 (1961).

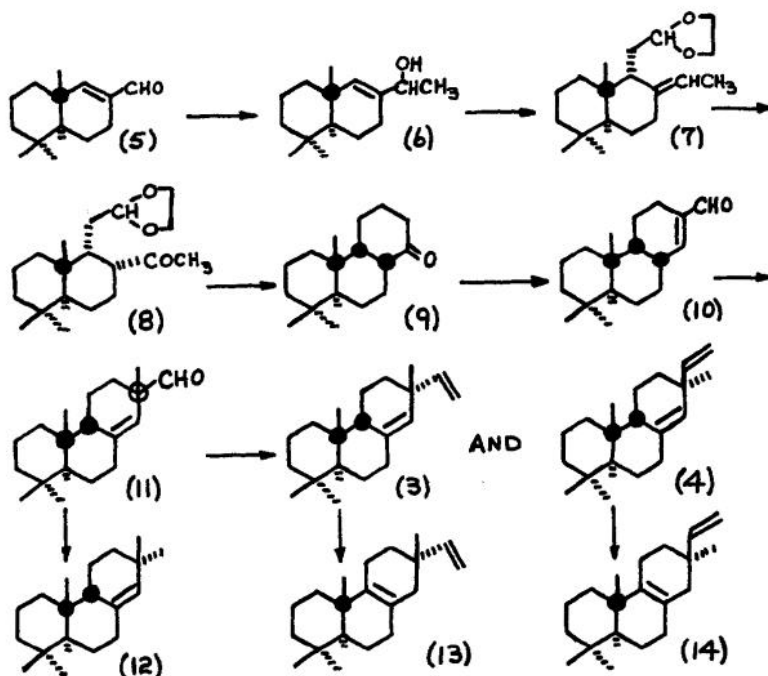
⁶ R. F. Church, R. E. Ireland and J. A. Marshall, Tetrahedron Letters No. 1, 34 (1961).

⁷ W. H. Watenabe and L. E. Conlon, J. Amer. Chem. Soc. 79, 2828 (1957).

⁸ A. W. Burgstahler and I. C. Nordin, J. Amer. Chem. Soc. 83, 198 (1961).

⁹ The stereochemistry of an aldehyde prepared in a similar fashion has been recorded⁰.

¹⁰ H. C. Brown, K. L. Marray, L. J. Murray, J. A. Snover and G. Zweifel, J. Amer. Chem. Soc. 82, 4233 (1960).



the keto acetal (8), m.p. 132-133.5° (C, 73.83%; H, 10.57%) was obtained in 60% yield. Acid cleavage of the acetal function and cyclization of the resulting aldehydoketone afforded a tricyclic α,β -unsaturated ketone, m.p. 116-117° ($\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 227 μ (E 8500); C, 82.75%; H, 10.44%) in 65% yield. On catalytic hydrogenation the saturated tricyclic ketone (9), m.p. 78-79.5° (C, 82.28%; H, 11.38%) was obtained in quantitative yield. Confirmation for the β -configuration of the 9-hydrogen atom was found in the non-identity of the ketone (9) with the trans-anti-trans-isomer, m.p. 78-80°, prepared in our earlier work² (infrared spectral comparison; depression of the melting point to 47-65° on admixture).

Introduction of the 13-methyl-13 vinyl substituents was

accomplished essentially as outlined previously² by conversion of the ketone (9) via the n-butylthiomethylene derivative¹¹ (m.p. 73-74°; C, 75.83%; H, 10.30%; S, 9.32%), and the α,β -unsaturated aldehyde (10), m.p. 107-109° (C, 83.08%; H, 10.91%) to the methylated aldehydes (11) in 43% overall yield, while separation of the epimeric aldehydes (11) by column chromatography proved unsatisfactory, pure samples of the 13-vinyl derivatives (3) (C, 87.93%; H, 11.76%) and (4) (C, 88.08%; H, 11.76%), prepared in quantitative yield from the aldehydes (11) by treatment with methylenetriphenylphosphorane¹², were readily available by preparative gas-liquid chromatography. When each diene was treated separately with dry hydrogen chloride in dry chloroform¹³ rearrangement of the nuclear double bond occurred, and the diene (3) afforded dl- $\Delta^{8(9)}$ -sandaracopimaradiene (13)¹⁴ (C, 88.12%; H, 11.92%), while the diene (4) yielded dl- $\Delta^{8(9)}$ -pimaradiene (14)¹⁴ (C, 88.05%; H, 11.75%), thus establishing the configuration at C(13) in the dienes (3) and (4). The NMR spectrum of the olefin (12) (C, 87.51%; H, 12.43%) (prepared by Wolff-Kishner reduction of the mixture of epimeric aldehydes (11)) showed a single, uncoupled vinyl hydrogen signal at 5.30 τ , thereby confirming the presence of a $\Delta^{8(14)}$ -double bond in the dienes

¹¹ R. E. Ireland and J. A. Marshall, J. Amer. Chem. Soc. 81, 6336 (1959).

¹² G. Wittig and V. Schöllkopf, Ber. 87, 1318 (1954).

¹³ O. E. Edwards and R. Howe, Canad. J. Chem. 37, 760 (1959).

¹⁴ Each of the reference $\Delta^{8(9)}$ -derivatives was prepared in a similar fashion in this laboratory from authentic samples of the corresponding pimaradiene.

(3) and (4). These observations coupled with the already demonstrated trans-syn-cis-phenanthrene skeleton of the ketone (9) conclusively establish the structure and stereochemistry of the dienes (3) and (4) as shown.

The lack of correspondence of the infrared spectra and mobility on gas-liquid chromatography of the diene (3) and isopimaradiene¹⁵, and the diene (4) and rimuene emphasized the incorrectness of the formulations of the natural substances.

These results necessitated a re-examination of the structures of rimuene and isopimaradiene, and it was found that these materials cannot be C(13) epimers as suggested⁵, since (a) isopimaradiene is readily rearranged by dry hydrogen chloride to $\Delta^{8(9)}$ -sandaracopimaradiene (13) while rimuene is unaffected by acid treatment; and (b) the behavior of rimuene and isopimaradiene on gas-liquid chromatography is inconsistent with their being only C(13) epimers and further suggests that isopimaradiene has the trans-anti-structure rather than the trans-syn-formulation now accepted (see Table I).

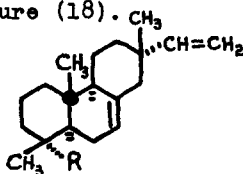
Table I

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

The observed acid-stability of rimuene suggests that it is a structural isomer of the pimaradienes rather than a

¹⁵ Prepared from isopimaric acid by the same sequence of reactions reported² earlier for sandaracopimaradiene and pimaradiene.

stereoisomer, as claimed⁵. On the other hand the acid-lability of isopimaradiene demonstrates its close relationship to the other pimaradienes. Inspection of the NMR spectrum of dihydroisopimaradiene (G, 87.73%; H, 12.38%) reveals two distinctive features not present in the spectra of the related dihydrodienes: (a) the presence of a broad, spin-coupled vinyl hydrogen signal at 5.03 τ (also evident in the NMR curve recorded for methyl isopimarate by Wenkert and Beak⁵) and (b) a strong signal at 8.32 τ best accommodated by the $-C=C-\underline{CH}_2-CR_3$ system. On the basis of these results and consideration of the proposed biogenesis of the resin acids¹⁶, we suggest that isopimaradiene is represented by structure (17) and hence isopimaric acid by structure (18).



(17) R=-CH₃ (18) R=-CO₂H

This structure is consistent with all the previous results recorded on isopimaric acid¹⁷ except the ozonolysis experiments¹⁸, for which there is no ready explanation. Experiments designed to obtain further chemical verification of this structural assignment are underway at present.

¹⁶ A. J. Birch, R. W. Richards, H. Smith, A. Harris and W. B. Whalley, Tetrahedron 7, 241 (1959).

¹⁷ A. K. Bose and W. A. Struck, Chemistry and Industry 1628 (1959); also see Edwards and Howe¹⁴ for a summary of earlier reports.

¹⁸ G. C. Harris and T. F. Sanderson, J. Amer. Chem. Soc. 70, 2081 (1948).