A Synthesis of 7-Isopimarene-18-oic Acid† (Dihydroisopimaric Acid)

By J. W. APSIMON

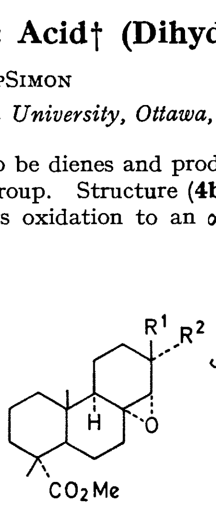
(*Department of Chemistry, Carleton University, Ottawa, Canada*)

Summary A synthesis is described of 7-isopimarene-18-oic acid (dihydroisopimaric acid) from methyl 8(14),15-isopimaradien-18-oate (methyl sandaracopimarate) based on the reactivity of α-epoxides in this series.

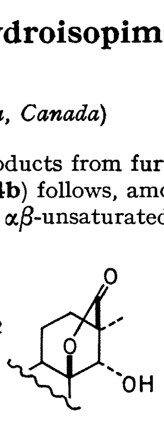
RECENTLY, we have demonstrated that α-epoxides derived from pimaric acid-type diterpenes are very reactive.[1] Thus (**1a**) reacts readily to give hydroxy-γ-lactone (**2**), our suggestion being that because of conformational factors, (**1**) exists largely with ring B in the boat form (**3**). In this manner the near side of the epoxide is revealed for attack by the carboxyl group, and the relief of non-bonded interactions in such a conformation would account for the instability of such α-epoxides.

In the case of the α-epoxide, (**1b**) derived from methyl 8(14), 15-isopimaradien-18-oate [methyl sandaracopimarate (**5a**)][2] unfavourable interactions cannot be relieved by lactone formation since the methoxycarbonyl group is not spatially disposed for ready attack. However, the 7β-hydrogen is ideally arranged for ready *trans*-elimination [arrows in (**3**)] leading to olefin (**4a**), one of the major products isolated directly from the epoxidation of the 8(14)-olefin corresponding to (**1b**).[3] This observation led us to devise a synthesis of the title acid (**5b**) thus providing for the first time a formal total synthetic entry into diterpenoids with a 7(8) double bond.[4]

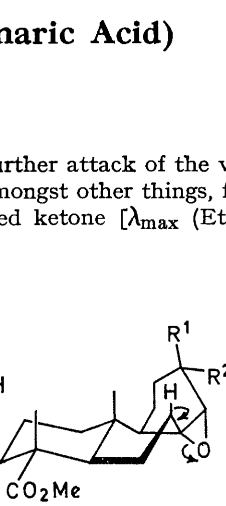
Methyl 8(14),15-isopimaradiene-18-oate, (methyl sandaracopimarate) was epoxidized with *m*-chloroperoxybenzoic acid in dichloromethane to give a mixture of products from which the 8,14β-epoxide was isolated (25%) together with the allylic alcohol (**4b**) (30%). No evidence for the 8,14-α-epoxide was obtained, the other products appearing mostly to be dienes and products from further attack of the vinyl group. Structure (**4b**) follows, amongst other things, from its oxidation to an $\alpha\beta$-unsaturated ketone [λ_{max} (EtOH) 246 nm, ϵ 6200; ν_{max} 1660 cm^{-1}] with manganese dioxide[6] and the appearance of the olefinic signal as a broadened doublet at δ 5·55 typical of $\Delta^{7(8)}$-diterpenes[4,7]. Pyridine-induced solvent shifts[8] indicated the α-orientation of the hydroxy-group.



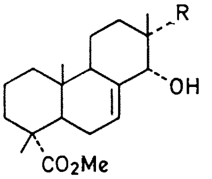
(**1**) a; R^1 = CO_2Me, R^2 = Me
b; R^1 = Me, R^2 = CO_2Me



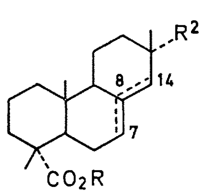
(**2**)



(**3**) a; R^1 = CO_2Me, R^2 = Me
b; R^1 = Me, R^2 = CO_2Me



(**4**) a; R = CO_2Me
b; R = $-CH=CH_2$



(**5**) a; R^1 = Me, R^2 = $-CH=CH_2$, $\Delta^{8(14)}$
b; R^1 = H, R^2 = Et, $\Delta^{7(8)}$

---

† The nomenclature used in this communication is based on a proposal of a number of diterpene chemists chaired by Dr. J. W. Rowe, Forest Products Laboratory, U.S. Department of Agriculture, Madison, Wisconsin 53705.

Reaction of (**4b**) with acetic anhydride and pyridine at 0° for 10 hr. gave the corresponding allylic acetate which with lithium in ethylamine[9] yielded 7-isopimarene-18-ol (dihydroisopimarinol) which on oxidation with an excess of Jones' reagent yielded the corresponding 18-oic acid (**5b**) in 50% yield, identical in all respects with an authentic sample. All new compounds exhibited the requisite analytical and spectral properties.

I thank the administrators of the C. D. Howe Foundation for a fellowship and Professor G. Ourisson, Institut de Chimie, Strasbourg, for his hospitality. Most of this work was performed while I was on leave in Strasbourg.

(*Received, November 10th*, 1969; *Com.* 1705.)

---

[1] J. W. ApSimon and H. Krehm, *Canad. J. Chem.*, 1969, **47**, 2859.

[2] J. W. ApSimon, A. S. Y. Chau, W. G. Craig, and H. Krehm, *Canad. J. Chem.*, 1967, **45**, 1439.

[3] J. W. ApSimon and H. Krehm, unpublished observations.

[4] W. Antkowiak, O. E. Edwards, R. Howe, and J. W. ApSimon, *Canad. J. Chem.*, 1965, **43**, 1257.

[5] A. Afonso, *J. Amer. Chem. Soc.*, 1968, **90**, 7375.

[6] L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, 1967, p. 636.

[7] E. Wenkert and P. Beak, *J. Amer. Chem. Soc.*, 1961, **83**, 998; A. W. Burgstahler, J. N. Marx, and D. F. Zinkel, *J. Org. Chem.*, 1969, **34**, 1550.

[8] P. V. Demarco, E. Farkas, D. Doddrell, B. L. Mylari, and E. Wenkert, *J. Amer. Chem. Soc.*, 1968, **90**, 5480; S. Hihashi, I. Yanagisawa, O. Tanaka, and S. Shibata, *Tetrahedron Letters*, 1969, 1682.

[9] A. S. Hallsworth, H. B. Henbest, and T. I. Wrigley, *J. Chem. Soc.*, 1957, 1969; J. A. Marshall and A. R. Hochstetler, *J. Org. Chem.*, 1966, **31**, 1020.