The Synthesis of Antipodal Polyalthic Acid from Levopimaric Acid[1]

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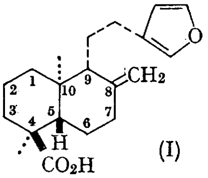
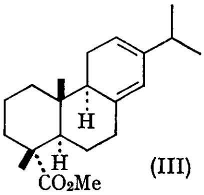
WE report the synthesis of the furano-diterpenoid system (VII) having the stereochemistry antipodal to that of polyalthic acid (I).[2] The starting point in the synthesis was the keto-acid ester (II) obtained by exhaustive ozonolysis of methyl levopimarate (III). The synthesis of (±)-(II) has been reported.[3]



(I)

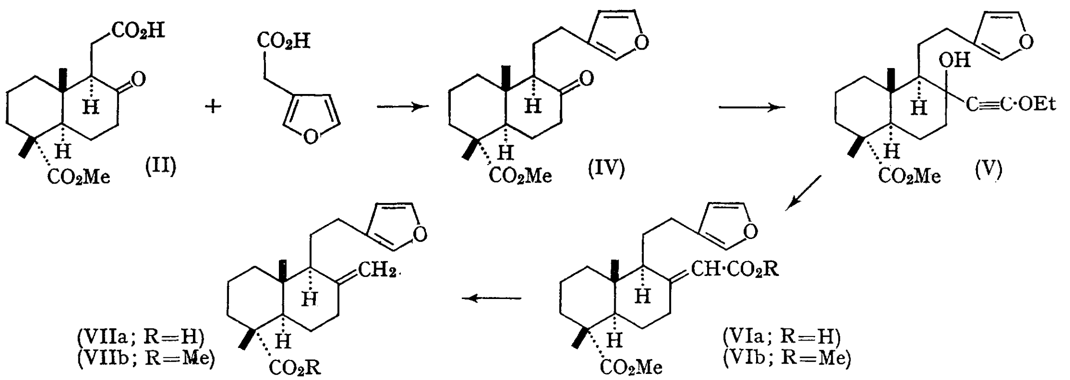


(III)

Ozonization of methyl levopimarate, m.p. 61—62° [lit.[4] 64—65°; λ_{max} 272·5 mμ (ε 5490)] in ethyl acetate at −40° followed by oxidation of the ozonide mixture with potassium permanganate in acetone gave the keto-acid ester (II),[5] m.p. 176—178° (lit.[6] 173—174°): ν_{max} (neat) 3448—2564, 1727, and 1712 (doublet), 1695 sh., cm.$^{-1}$; n.m.r. ($CDCl_3$): τ 9·21 (3H singlet), 8·81 (3H singlet), 6·31 (3H singlet), and 1·62 (broad singlet, CO_2H), in yields varying from 20—45%.

Elaboration of the C-9 side chain bearing the furan ring was accomplished by Kolbe electrolytic coupling[7,8] of (II) and 3-furylacetic acid.[9] The 3-furylacetic acid employed in the electrolysis was prepared from 3-furoic acid[9] according to the Arndt–Eistert method.[10]

When the mixture of keto-acid ester (II) and 3 furylacetic acid in dimethylformamide containing triethylamine was electrolyzed using smooth platinum electrodes the desired keto-ester (IV), [m.p. 93—96°; ν_{max} (CCl_4) 1732, 1720, 1493, 1021, and 873 cm.$^{-1}$; n.m.r. (CCl_4) τ 9·28 (3H singlet), 8·87 (3H singlet), 6·41 (3H singlet), 3·88 (1H multiplet), 2·94 (1H multiplet), 2·81 (1H multiplet)] was formed as one of the products. Elaboration of the exocyclic methylene group was accomplished by the Stork procedure[8,11] by treatment of (IV) with lithium ethoxyacetylide at −20° to give the acetylenic carbinol (V): ν_{max} (CCl_4) 3500, 2262, 1727, 1495, 873 cm.$^{-1}$, which without purification was converted into the required αβ-unsaturated ester (VIb) [ν_{max} (CCl_4) 1724, 1637, 1493, and 875 cm.$^{-1}$; λ_{max} (EtOH) 220 mμ (20,000)] by treatment with methanolic 10% sulphuric acid in a yield of 60% from (IV). Heating (VIb) under reflux with aqueous methanolic potassium hydroxide gave the unsaturated acid (VIa) in 80% yield, which without purification was decarboxylated[8] to (VIIb) by heating in quinoline containing copper chromite.[12] The olefinic ester (VIIb): ν (CCl_4) 1724, 1639, and 893, 1495, and 873 cm.$^{-1}$, was smoothly hydrolyzed to the corresponding antipodal polyalthic acid (VIIa): [m.p. 98—99°; ν (CCl_4) 1692, 1638 and 895, 1495 and 874 cm.$^{-1}$; n.m.r. ($CDCl_3$) τ 9·3 (3H singlet), 8·8 (3H singlet), 8·3 (multiplet, methylene protons), 5·4 (1H multiplet, olefinic proton), 5·1 (1H multiplet, olefinic proton), 3·7 (1H multiplet, β-proton on furan ring), 2·8 and 2·6 (1H multiplet for both α-protons on furan ring)] by treatment with potassium t-butoxide in dimethyl sulphoxide.[13] The infrared ($CHCl_3$ and Nujol mull), n.m.r. ($CDCl_3$), and mass spectra of the acid (VIIa) were



identical in all respects with those of a natural sample of polyalthic acid as was also the behaviour of the two samples on thin-layer silica gel chromatoplates in ethyl acetate–benzene–ether (1 : 3 : 0·1).

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[1] Part of a dissertation by L. B. Hawley, Jr. submitted to the Graduate School in partial fulfilment of the requirements for the Ph.D. in Chemistry.

[2] K. W. Gopinath, T. R. Govindachari, P. C. Parthasarathy, and N. Viswanathan, *Helv. Chim. Acta*, 1961, **44**, 1040.

[3] See accompanying Communication, p. 94.

[4] V. Loeblich, D. Baldwin, R. O'Conner, and R. V. Lawrence, *J. Amer. Chem. Soc.*, 1955, **77**, 6311.

[5] Satisfactory analytical data were obtained for all compounds reported in this Communication. Melting points are corrected.

[6] L. Ruzicka, E. Bernold, and A. Tallichet, *Helv. Chim. Acta*, 1941, **24**, 223.

[7] L. Rand and A. F. Mohar, *J. Org. Chem.*, 1965, **30**, 3885.

[8] G. Stork, A. Meisels, and J. E. Davies, *J. Amer. Chem. Soc.*, 1963, **85**, 3419. This electrolytic coupling is analogous to that used in the Stork onocerin synthesis, except that the Stork synthesis involved symmetrical coupling.

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[10] M. S. Newman and P. F. Beal, *J. Amer. Chem. Soc.*, 1950, **72**, 5163.

[11] N. Danieli, Y. Mazur, and F. Sondheimer, *Tetrahedron Letters*, 1961, 310.

[12] H. Adkins and R. Conner, *J. Amer. Chem. Soc.*, 1931, **53**, 1091.

[13] F. C. Chang and N. Wood, *Tetrahedron Letters*, 1964, 2969.