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SYNTHESIS OF ERYTHROXYDIOL A (HYDROXYMONOGYNOL)*

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Erythroxydiol A (hydroxymonogynol, IX) is a diterpene isolated from Erythroxylon monogynum by two groups of workers (1-3). The presence of a bridgehead hydroxymethyl group at C-13 of this diol is the unique characteristic common to some tetracyclic diterpenes of beyerane group. Here we describe its synthesis using an interesting skeletal rearrangement (II → III) recently discovered in the gibberellin field (4,5).

(-)-Steviol methyl ester (Ib)(6), prepared from (-)-steviol (Ia), was oxidized with m-chloroperbenzoic acid in benzene-dioxan to give an epoxide (II), m.p. 144-145° (7). Upon treatment with a trace of hydrochloric acid in aqueous acetone this kaurane epoxide (II) afforded a beyerane ketol (III), m.p. 171-172°, ν_{max} (Nujol) ~3500, 1735 (sh), 1705 (br.) cm^{-1}. δ (ppm from TMS at 100MHz, $CDCl_3$) 0.70 (3H, s), 1.19 (3H, s), 2H AB_q (J=12Hz) centered at 3.46 and 3.63, 3.62 (3H, s). Jones chromic acid oxidized the ketol (III) to a keto acid (IVa), m.p. 205-206°. The corresponding methyl ester (IVb), m.p. 168-169°, was obtained by esterification with diazomethane. This was treated with sodium borohydride in ethanol to give a single crystalline hydroxy ester (V), m.p. 143-144° (cf. 8). Its mesylation with mesyl chloride in pyridine gave an oily crude mesylate (VI) contaminated with some chloro compound (VII). This was heated with collidine under reflux to give a crude mixture of VII and an unsaturated ester (VIII) which was separated by chromatography over alumina. The chloro compound (VII) was heated with lithium bromide and lithium carbonate in DMF to afford an additional amount of the ester (VIII) as a crude crystalline substance readily soluble in light petroleum, δ 0.63 (3H, s), 1.22 (3H, s), 3.63 (3H, s), 3.67 (3H, s), 2H AB_q (J=6Hz) centered at 5.75 and 5.87. Reduction of the diester (VIII) with lithium aluminum hydride gave erythroxydiol A (IX), m.p. 180-

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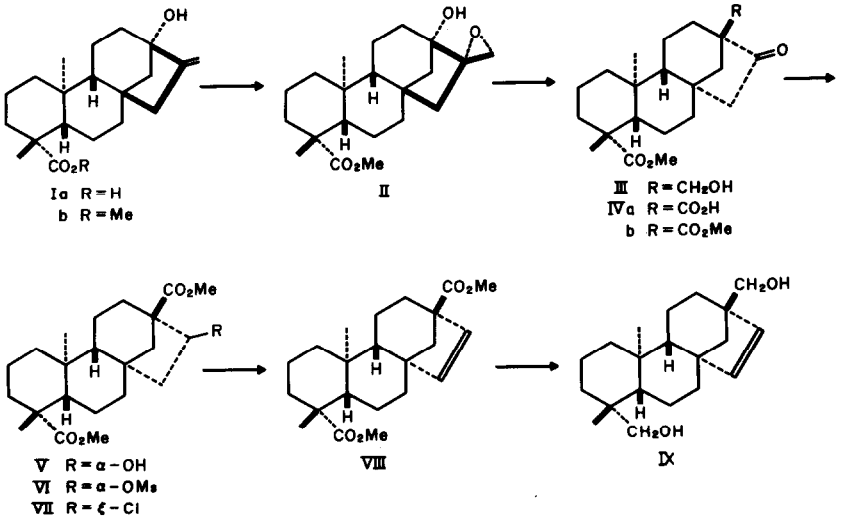
* Diterpenoid Total Synthesis. Part XV. Part XIV, K. Mori, Y. Nakahara and M. Matsui, Tetrahedron Letters, in the press.



181°, δ 0.75 (3H, s), 0.99 (3H, s), 3.48 (2H, br. s), 2H AB_q (J=12Hz) centered at 3.44 and 3.77, 2H AB_q (J=6Hz) centered at 5.56 and 5.78. This was indistinguishable from the natural product on the basis of m.m.p., IR, NMR, MS, ORD (plain positive curve) and TLC.

Since the total synthesis of (±)-steviol (Ia) has been reported by us (9), this work constitues a formal total synthesis of (±)-erythroxydiol A.

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