Tetrahedron Letters No.18, pp. 2215-2217, 1968. Pergamon Press. Printed in Great Britain.

A DIRECT CORRELATION OF (+)-MALABARICOL WITH (+)-AMBREINOLIDE

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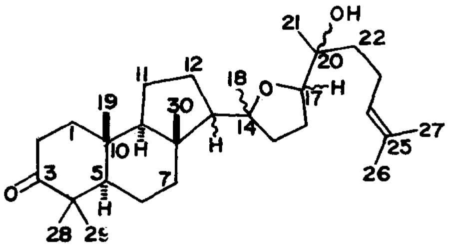
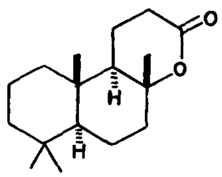
(Received in UK 17 January 1968)

IN a recent publication[1] we have described the isolation and structure determination of malabaricol and related compounds, which constitute a new class of triterpenoids. Except for a suggestion, based on the CD of malabaricol and the octanor-γ-lactone derived from this, that the A/B rings may be trans-fused, no stereochemical conclusions were drawn. We now report on a direct correlation of (+)-malabaricol with (+)-ambreinolide (II), a compound with a well-secured absolute stereo-structure[2], which besides providing additional independent structural proof for the rings A,B and C and the four quaternary methyls, defines the absolute stereochemistry of malabaricol and its congeners at C_5, C_8, C_9 and C_{10} as depicted in I for (+)-malabaricol.

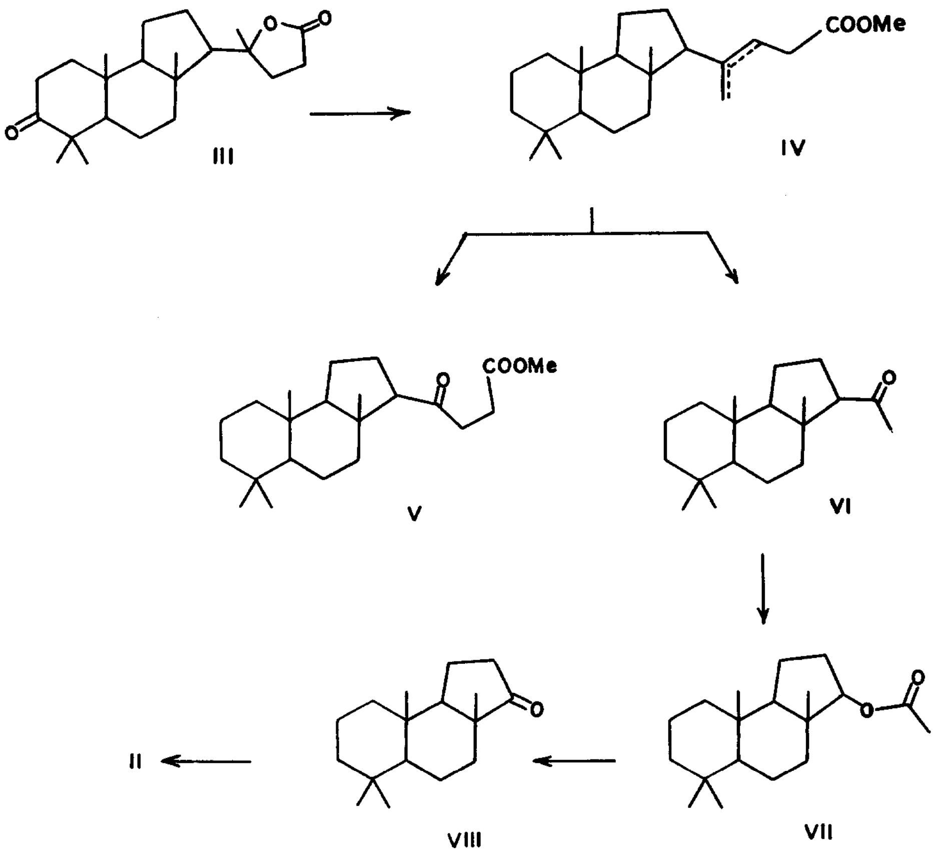


I



II

Octanor-γ-lactone (III)[1], under the conditions of Wolff-Kishner reduction[3], underwent both the reduction of the C_3-carbonyl and dehydration[4] of the C_{14}-tertiary OH (derived from the lactone opening under the alkaline reaction conditions) to furnish in ~ 60% yield a mixture of olefinic acids, which was characterised as its methyl ester (IV) by PMR[5]: $-C{=}C\underline{H}_2$, two singlets at 279 and 293 c/s; $-C{=}C\underline{H}-CH_2$, triplet centred at 310 c/s, J = 8 c/s; $-C{=}CH-C\underline{H}_2-COOMe$, doublet centred at 181 c/s, J = 8 c/s. This methyl esters mixture, without separation, was ozonolysed to give two products (V,VI) in almost equal amounts; their mixture was readily resolved by a column chromatography over SiO_2 gel. The less polar product was the desired methyl ketone (VI), m.p.69-70°,



$\nu^{c=o}_{Nujol}$ 1715 cm^{-1}; PMR: quaternary methyls (9H singlet at 50 c/s and, 3H singlet at 61 c/s), $C\underline{H}_3CO$ (3H singlet at 121 c/s), $CH_3COC\underline{H}$- (1H, ill-defined multiplet centred at 155 c/s).

The above methyl ketone on Baeyer-Villiger oxidation with perbenzoic acid in benzene (72 hr at ~10°) furnished the corresponding acetate (VII), m.p. 110-111°, $\nu^{c=o}_{Nujol}$ 1738 cm^{-1}; PMR: quaternary methyls (3H singlet at 51 c/s and, 9H singlet at 53 c/s), $C\underline{H}_3COO$ (3H singlet at 114 c/s), CH_2-$C\underline{H}$-OAc (1H doublet centred at 276 c/s, J = 6 c/s). The acetate was saponified and the resulting alcohol (m.p. 138.5-139.5°; IR in Nujol: OH 3300, 1000, 975 cm^{-1}) oxidised by Jones reagent[6] to give the ketone VIII, m.p. 98-98.5°, $\nu^{c=o}_{CCl_4}$ 1742 cm^{-1}; M$^+$ at m/e = 248; PMR, quaternary methyls (two 6H singlets at 52 and 57 c/s), $C\underline{H}_2CO$ (2H multiplet centred at 135 c/s). This ketone (VIII) on prolonged exposure to perbenzoic acid yielded in ~ 50% yield a product (m.p. 142-143, $[\alpha]^{30}_D$ +28° in $CHCl_3$) identified (mixed m.p., TLC, IR) as (+)-ambreinolide (II; Lit.[7]: m.p. 142-144°, $[\alpha]_D^{20}$ +33.3° in $CHCl_3$).

The ketone VIII displays a strong negative Cotton effect ($\Delta\varepsilon_{301}$ -3.648, Γ = 38 mμ ; dioxane) in its CD curve. This information and the earlier results[1] on the CD of malabaricol and the octanor-γ-lactone, when utilised to deduce the absolute stereochemistry of the A/B/C ring junctions, lead to the same conclusions as already reached above.

Acknowledgement - The authors are grateful to Prof.E.J. Corey for a sample of (+)-ambreinolide and to Prof. G. Ourisson for the CD curves.

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