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A SIMPLIFIED ROUTE TO A KEY INTERMEDIATE IN THE TOTAL SYNTHESIS OF α-ONOCERIN[1]

Naftali Danieli, Yehuda Mazur and Franz Sondheimer

Daniel Sieff Research Institute, Weizmann Institute of Science, Rehovoth, Israel

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dl-1,1,10β-Trimethyl-trans-decal-2β-ol-6-one-5-acetic acid (VI) is a key intermediate in the total synthesis of α-onocerin of Stork et al.,[2] since it can be converted to this naturally occurring triterpene by successive resolution, electrolytic coupling and transformation of the carbonyl to methylene groupings.[2] Very recently Church et al.[3] have described an alternative synthesis of the acid (VI) by a route which proceeds from the keto-benzoate (I) first prepared in our laboratories.[4] This latter publication prompts us now to report a new and much more direct method for carrying out the conversion of (I) to (VI). Our synthesis of (VI) moreover involves fewer steps than that of Stork et al.[2] and is therefore the shortest one available.

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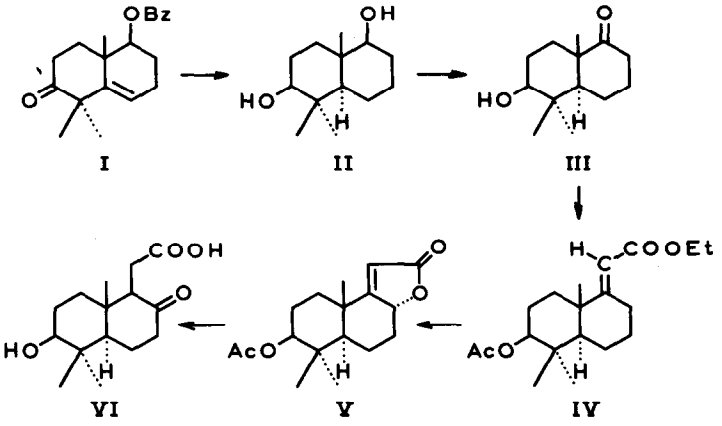
[1] For previous work in this series see F. Sondheimer and M. Gibson, Bull.Res.Counc.Israel 9A, 204 (1960).

[2] G. Stork, J. E. Davies and A. Meisels, J.Amer.Chem.Soc. 81, 5516 (1959).

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

[4] F. Sondheimer and D. Elad, J.Amer.Chem.Soc. 79, 5542 (1957).



The keto-benzoate (I)[4] on saponification and subsequent hydrogenation of the resulting keto-alcohol[5,6] in acetic acid over platinum yielded 85%[7] of the saturated diol (II) (m.p. 180-182°; Found: C, 73.33; H, 11.26). Partial oxidation with 1.2 equivalents of chromium trioxide in pyridine gave the known keto-alcohol (III) (m.p. 72-74°)[5,8,9,10] in 45% yield (based on unrecovered diol); reduction with lithium aluminum hydride of the other oxidation products then brought the yield of (III) to 80%.[11]

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5 F. Sondheimer and D. Elad, J.Amer.Chem.Soc. 80, 1967 (1958).

6 J. D. Cocker and T. G. Halsall, J.Chem.Soc. 3441 (1957).

7 Yields are given to the nearest 5%.

8 J. Kalvoda and H. Loeffel, Helv.Chim.Acta 40, 2340 (1957).

9 B. Gaspert, T. G. Halsall and D. Willis, J.Chem.Soc. 624 (1958).

10 N. B. Haynes and C. J. Timmons, Proc.Chem.Soc. 345 (1958).

11 The present 3-step method for transforming (I) to (III) is considerably simpler than the one described by us previously.[5]

Acetylation of (III), followed by condensation with lithium ethoxyacetylide in ether and then treatment with 5% methanolic sulfuric acid at room temperature, afforded 55% of the αβ-unsaturated ester (IV) [m.p. 85-86° and 99-100° (polymorphic forms); λ_{max}^{EtOH} 221 m (ε 13,400); infrared bands (KBr) at 1739, 1718 and 1640 cm^{-1}; Found: C, 70.74; H, 9.37]. Oxidation with selenium dioxide in boiling acetic acid produced the αβ-unsaturated γ-lactone (V) [m.p. 129-130°; λ_{max}^{EtOH} 215 m (ε 11,900); infrared bands (KBr) at 1757, 1736 and 1640 cm^{-1}; Found: C, 69.67; H, 8.12] in 75% yield. Finally, treatment with 20% potassium hydroxide in boiling aqueous ethylene glycol led to 55% of the acid (VI) (m.p. 185-186°) which proved to be identical (mixture m.p., infrared comparison) with a sample kindly provided by Dr. A. Meisels. The corresponding methyl ester (m.p. 110-111°) likewise was identified with an authentic sample.