

## Pentacyclic Triterpene Synthesis. Preparation of a Useful Intermediate

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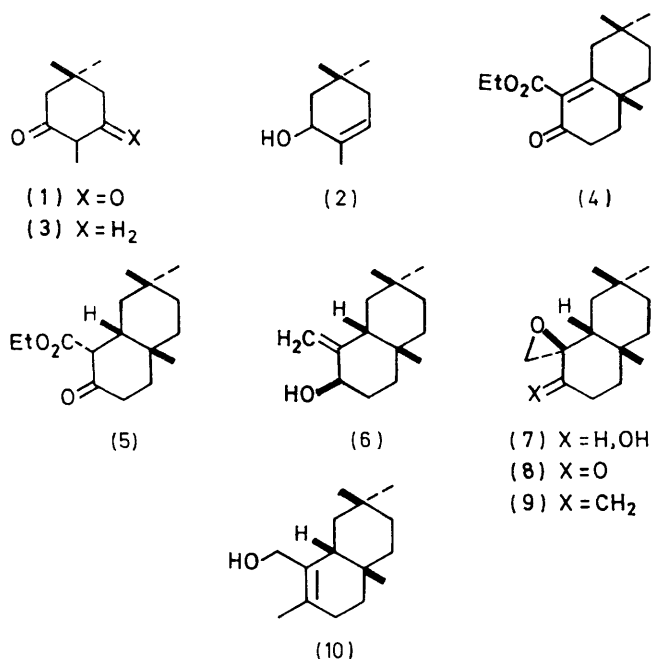
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**Summary** 3,4,4a,5,6,7,8,8a $\beta$ -Octahydro-2,4a $\beta$ ,7,7-tetramethylnaphthyl-1-methanol, a useful intermediate for further elaboration into the pentacyclic triterpene  $\beta$ -amyrin, has been synthesized in a ten-step route from 2,5,5-trimethylcyclohexane-1,3-dione.

WE report the synthesis of the allylic alcohol (10), a useful intermediate for further elaboration into the pentacyclic triterpene  $\beta$ -amyrin.

2,5,5-Trimethylcyclohexane-1,3-dione (1)<sup>1</sup> was reduced with lithium aluminium hydride in ether at room tempera-

ture to obtain allylic alcohol (2) in 85% yield. Oxidation of (2) (sodium bichromate in aqueous sulphuric acid-benzene at 0°), followed by catalytic hydrogenation of the resulting enone (palladized carbon in ethyl acetate) gave the ketone (3) in 76% yield.



Treatment of the ketone (3) with a 15 mole % excess of ethyl 5-ethoxy-3-oxovalerate<sup>2</sup> and toluene-*p*-sulphonic acid in refluxing benzene produced the unsaturated keto-ester (4), m.p. 97.5–98.5°, in 49% yield.† Catalytic hydrogenation of (4) (palladized carbon in ethyl acetate) gave the keto-ester (5), m.p. 35–38° in quantitative yield. The stereochemistry of (5) was shown by its conversion into *cis*-2,2,4a-trimethyldecalin.‡

Lithium aluminium hydride reduction of (5) afforded the allylic alcohol (6), m.p. 82–83° in 91% yield.§ Compound (6), on treatment with *m*-chloroperoxybenzoic acid in chloroform at room temperature, gave the epoxy-alcohol (7), m.p. 90.5–92° in 98% yield. Jones oxidation<sup>6</sup> of the epoxy-alcohol (7) gave the epoxy-ketone (8), m.p. 93–94°, in 81% yield. The ketone (8), on treatment with methylenetriphenylphosphorane (2 equiv.) in dimethyl sulphoxide<sup>7</sup> at 75° for 19 h, afforded the liquid epoxy-olefin (9) [<sup>1</sup>H n.m.r. (CCl<sub>4</sub>) τ 9.17, 9.10, 8.90 (methyl singlets), 7.62, 7.42 (each a one-proton doublet, *J* 7 Hz, oxiran protons), 5.40, and 5.20 (each a broadened one-proton singlet, vinyl protons)] in 74% yield.¶ Reduction of (9) with lithium in ethylamine (10% excess of lithium, room temperature) gave the allylic alcohol (10) [liquid, <sup>1</sup>H n.m.r. (CCl<sub>4</sub>) τ 9.14, 9.10, 9.06, 8.38 (methyl singlets), 6.24, and 5.94 (each a one-proton doublet, *J* 11 Hz, carbonyl protons)] in 98% yield.

We thank the National Science Foundation and the University of California Committee on Research for financial support.

(Received, September 16th, 1971; Com. 1614.)

† Although the yield in this reaction is rather low, there is no other known method for accomplishing this conversion (3 → 4) in such a direct manner. Although the acid-catalysed equivalent of the well known Robinson–Mannich annelation sequence is rarely used, it offers definite advantages in certain cases such as this. With more highly activated ketones, yields are much higher *i.e.*, the β-diketone (1) is transformed into the corresponding annelation product in over 80% yield.

‡ *cis*-2,2,4a-Trimethyldecalin was prepared by Wolff–Kishner reduction of either *cis*-2,2,4a-trimethyl-7-decalone<sup>4</sup> or *cis*-2,2,4a-trimethyldecalin-4,7-dione.<sup>5</sup> Conversion of the latter dione into a tricyclo[4,4,0,0<sup>2,7</sup>]decane derivative confirms its *cis*-stereochemistry.

§ The yield quoted is for the crude product. We normally use the unpurified reduction product, which contains about 10% of an isomer, directly in the subsequent transformation. All other yields quoted are for material of analytical purity. The stereochemistry of this compound was assigned on the basis of its <sup>1</sup>H n.m.r. spectrum.

¶ This sensitive Wittig reaction must be performed under scrupulously anhydrous conditions in order to avoid destruction of the epoxy-ketone.

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<sup>2</sup> I. N. Nazarov and S. I. Zav'yalov, *Zhur. obshchei Khim.*, 1953, 23, 1703. This intermediate is more conveniently prepared by acylation of the magnesium salt of ethyl hydrogen malonate with 0.5 equiv. of 3-ethoxypropionyl chloride in tetrahydrofuran. (Yield: 60%) (Cf. ref. 3).

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<sup>5</sup> C. H. Heathcock and D. Gray, *Tetrahedron*, 1971, 27, 1239.

<sup>6</sup> K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1946, 39.

<sup>7</sup> R. Green, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, 1963, 28, 1128.