

SYNTHESIS OF 3 $\beta$ ,6 $\alpha$ -DIHYDROXY-5 $\alpha$ -PREGN-9(11)-EN-20-ONE

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Steroidal saponins obtained from starfish of various species contain the novel 3 $\beta$ ,6 $\alpha$ -dihydroxy-9(11)-ene system,<sup>1-4</sup> and the double bond in ring C appears to be characteristic of starfish saponins in the same way as ring B unsaturation characterises the free sterol content.

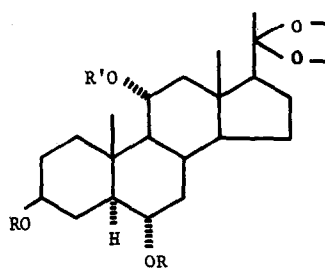
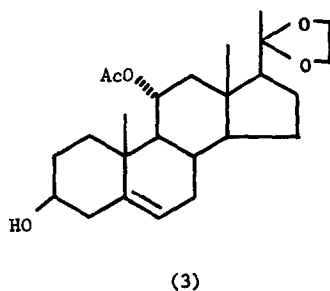
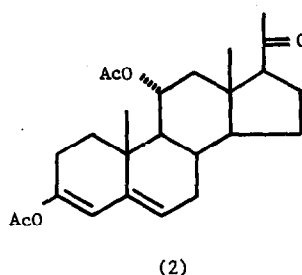
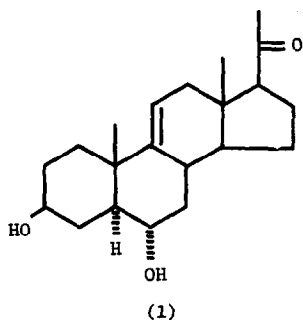
The title compound (1) has recently been shown to be the main aglycone of Asterias amurensis saponins,<sup>2</sup> and has also been isolated from extracts of the starfish, Acanthaster planci<sup>3,4</sup> and Asterias forbesi.<sup>4</sup> We now report the synthesis of this pregnane derivative and its identification as a minor component of the saponins of the starfish, Marthasterias glacialis, and as a major aglycone of the saponin fraction of the common starfish, Asterias rubens.

Treatment of 11 $\alpha$ -hydroxyprogesterone with excess of isopropenyl acetate in refluxing benzene, containing toluene-p-sulphonic acid as catalyst, gave the dienol diacetate (2). Ketalization at C-20, followed by cleavage and reduction of the dienol acetate with sodium borohydride in aqueous ethanol<sup>5</sup> gave the 5-en-3 $\beta$ -ol (3), m.p. 152-154°, in overall yield of 50%. Hydroboration-oxidation of this olefin gave, after t.l.c. separation from the 6 $\beta$ -epimer, the 3 $\beta$ ,6 $\alpha$ -diol (4), m.p. 221-222°, in 25% yield. Final transformation of the diol (4) to the  $\Delta^9(11)$ -derivative (1) was achieved without isolation of intermediates by protection of the hydroxyl groups in the form of their tetrahydropyranyl ethers. The di-tetrahydropyranyl ether (5) was converted into the alcohol (6) in refluxing methanolic potassium hydroxide. Formation of the tosylate (7), followed by elimination of toluene-p-sulphonic acid by means of sodium acetate in acetic acid, and final hydrolysis of the partially acetylated olefin with methanolic potassium hydroxide at room temperature yielded 3 $\beta$ ,6 $\alpha$ -dihydroxy-5 $\alpha$ -pregn-9(11)-en-20-one (1). After t.l.c. purification and crystallisation from ethyl acetate-hexane, it had m.p. 150-153°, mixed m.p. 150-153° with a sample of the natural material.\* Identity was verified by g.l.c. and t.l.c., and by comparison of n.m.r., i.r. and mass spectral data.

The diol (1) was shown by g.l.c. and spectral measurements to be present as a minor

component in the aglycone mixture obtained from the saponins of the starfish, Marthasterias glacialis. Similar methods have established that it is also present as a major component in the hydrolysate from extracts of the starfish, Asterias rubens. The aglycone mixture from this source contains four main components (ratio 9:9:3:1 by g.l.c.). The other principal constituent has been identified as dihydromarthasterone, [3 $\beta$ ,6 $\alpha$ -dihydroxy-5 $\alpha$ -cholest-9(11)-en-23-one], which has previously been obtained from extracts of M. glacialis<sup>1</sup> and A. amurensis.<sup>6</sup>

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- (4) R = H; R' = Ac  
 (5) R = THP; R' = Ac  
 (6) R = THP; R' = H  
 (7) R = THP; R' = Tosyl

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