11α,12α-EPOXY-3,20-DIOXOPREGNANE

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In the course of work on the preparation of steroids with a ruptured C-ring, 3,20-dioxo-Δ^{11}-pregnene was oxidized with chromic acid. The reaction was carried out at room temperature in aqueous acetic acid – sulfuric acid, using equimolar proportions of steroid and oxidizing agent to provide 60–70% of a crude, crystalline product. Spectrophotometric examination in the infrared region showed the absence of hydroxyl, acetoxyl, carboxyl, and aldehyde groups; there was, however, an indication of the presence of epoxide absorption as evidenced by two medium-sized bands at 805 cm^{-1} and 878 cm^{-1}. Elemental analyses of the purified compound agreed with the formula for 11,12-epoxy-3,20-dioxopregnane. The n.m.r. spectrum showed the presence of an AB type pattern in the region of 3 p.p.m., characteristic of steroidal 11,12-epoxides; the chemical shifts (δ, 2.98 and 3.14 p.p.m.) and coupling constants ($J_{11,12} = 4$, and $J_{9,11} = 0$ c.p.s.) are in excellent agreement with values reported (1) for 11α,12α-epoxides, but not for the corresponding β-epoxides. Reduction of the unknown with lithium aluminium hydride and subsequent oxidation of the product with chromic acid provided 70% of 3,12,20-trioxopregnane (2). This evidence gives further support for the α-configuration of the epoxide; it is known (3, 4) that the lithium aluminium hydride reduction of a steroidal 11α,12α-epoxide, such as 3β-acetoxy-11α,12α-epoxy-5α,22*a*-spirostane, yields the corresponding 12α-hydroxy compound, while 11β,12β-epoxides provide (5, 6) 11β-hydroxy steroids. These results agree with the concept (7) of axial attack on an epoxide by aluminiohydride ions via an S_N2 mechanism, the product having the hydroxyl group in the axial position. An exception to this rule seems to have been observed (5, 8) in the lithium aluminium hydride reduction of methyl 3α-acetoxy-11α,12α-epoxycholanate to 3α,11α,24-trihydroxycholane.*

The reaction of isolated double bonds with chromic acid is a complex one, but there are many indications that epoxides are formed as final or intermediary products. Chromic acid oxidations of 2,4,4-trimethylpent-1-ene (9), 2,4-dimethylpent-2-ene (10), and 1,1-diphenyl-2-methyl-prop-1-ene (11) gave good yields of the corresponding epoxides. In the steroid field, chromic acid oxidation of 5α-hydroxy-6β,16α-dimethyl-$\Delta^{6,7}$-pregnenolone 3-acetate yielded (12) the corresponding 6α,7α-epoxide, and $\Delta^{8,14}$-cholestenyl acetate (13) as well as $\Delta^{8,14}$-ergostenyl acetate (14) afforded a mixture of products including the 7-oxo- and 15-oxo-8α,14α-epoxides.

EXPERIMENTAL

11α,12α-Epoxy-3,20-dioxopregnane

A solution of chromic acid (1 g) in water (2 ml), acetic acid (25 ml), and sulfuric acid (1 ml) was added within 10 min to a solution of 3,20-dioxo-Δ^{11}-pregnene (3.15 g) in acetic acid (25 ml). During this addition, the mixture first turned cloudy, and then a green–black, gummy precipitate formed. As soon as all of the oxidizing solution had been added, the mixture was diluted with water (100 ml). This addition of water was made in several portions over a period of 10–15 minutes, and the gummy precipitate gradually dissolved to give a clear, green solution. A precipitate settled out shortly after the addition of water had been completed; after ½ h, the precipitate was filtered off, washed with water, and vacuum dried at 70° to provide 1.28 g of material, m.p. 142–152°. Dilution of the filtrate with more water (35 ml) yielded an additional

**A personal communication from Ciba Ltd., received since acceptance of this manuscript, states that an error was made in U.S. patent 2,599,481 and in corresponding patents issued in other countries, and that the lithium aluminium hydride reduction of methyl 3α-acetoxy-11α,12α-epoxycholanate actually yields 3α,12α,24-trihydroxycholane.*

0.82 g of solid, m.p. 147–153°. The two crops were combined and charcoal added. Recrystallization from ethyl acetate gave 1.47 g of crystals, m.p. 170–178°. Two further recrystallizations from this solvent raised the melting point to 182–185°; $[\alpha]_D^{25}$ +78.1° (*c*, 0.598, dioxane).

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15; O, 14.53. Found: C, 76.50, 76.29; H, 9.18, 9.18; O, 14.68, 14.59.

3,12,20-Trioxopregnane

Lithium aluminium hydride (0.57 g) and 11α,12α-epoxy-3,20-dioxopregnane (1 g) were refluxed in ether (100 ml) for 4 h. An additional 0.75 g of reducing agent was then added, and refluxing was continued for 4 more hours. The cooled mixture was decomposed by dilute acetic acid and then poured into dilute hydrochloric acid, and the products were extracted with ether. After washing and evaporation of the solvent extract, the residue (0.9 g) was dissolved in acetic acid (20 ml) and water (2 ml). This solution was then treated dropwise, over a period of 15 min, with a solution of chromic acid (0.8 g) in water (10 ml), acetic acid (40 ml), and sulfuric acid (1 ml). After 15 h the mixture was poured into water, the products were extracted with ether – methylene chloride, and the solvent extract was worked up in the usual way. The residue (0.85 g) was crystallized from ether to give 0.67 g of material, m.p. 190–192°. Two further recrystallizations from ether and acetone gave pure 3,12,20-trioxopregnane, m.p. 198–201°, giving no depression on admixture melting point, and exhibiting an infrared spectrum which was superimposable on that of an authentic sample of this compound.

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THE ALKALOIDS OF FUMARIACEOUS PLANTS. LII. A NEW ALKALOID, CULARICINE, AND ITS STRUCTURE

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The author (1) has described an investigation of the alkaloids of *Corydalis claviculata* (L.) DC. in which an amorphous phenolic fraction was obtained. At the time of publication it had not been possible to isolate pure individual bases from this fraction although it was shown to consist, to a large extent, of a base or bases which on O-methylation generated cularine. It has now been possible to isolate two phenolic bases and to determine the structure of one of these, namely that of cularicine. The other base proved to be identical with cularidine which had already been obtained from *Dicentra cucullaria* (L.) Bernh. (2).

The empirical formula of cularicine, $C_{18}H_{17}O_4N$, suggests that it might be cularidine or an isomer in which two methoxyls have been replaced by a methylenedioxy group and