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### 5 $\alpha$ -HYDROXY-3 $\alpha$ -CHOLESTANECARBOXYLIC LACTONE

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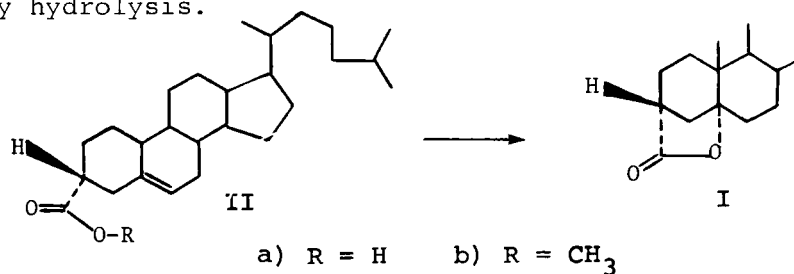
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5 $\alpha$ -HYDROXY-3 $\alpha$ -CHOLESTANECARBOXYLIC LACTONE

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Given the large number of synthetic lactones as well as those isolated from natural sources in recent years, it is surprising that compound I has not been reported.<sup>1</sup> Several years ago<sup>2</sup> we noted a slow isomerization (IR) of the 3 $\alpha$ -acid (IIa), presumably to I. We have now prepared this lactone (I). After the requisite 3 $\alpha$ -acid (IIa) was obtained from the 3 $\beta$ -acid via a procedure essentially equivalent<sup>2</sup> to that used by Shoppee and Stephenson,<sup>3</sup> I was synthesized directly from IIa as well as from IIb by hydrolysis.

EXPERIMENTAL<sup>4</sup>

Procedure A (from IIa).— The necessary 3 $\alpha$ -acid was prepared according to a procedure used by Wintersdorf,<sup>2</sup> starting with cholesteryl chloride instead of cholesteryl bromide used earlier by Shoppee and Stephenson.<sup>3</sup> To a solution made up of 4.5 ml of dioxane, 0.44 ml of water and 0.56 ml of perchloric acid (90% aqueous dioxane, 0.2 N in perchloric acid) was added 100 mg of IIa. The mixture was placed in a long stem flask, which was filled with argon gas and placed in a Dry Ice-acetone bath

while the stem was drawn off and sealed. The flask was placed in an oil bath at 80° for ten days. At the end of this period the contents were poured into an evaporating vessel and the liquid removed under reduced pressure (25°). The residue was mixed with 25 ml of 2 N cold sodium hydroxide<sup>5</sup> and extracted three times with 50 ml portions of ether, separating any suspended material along with the aqueous phase. The ethereal extracts were combined and washed with cold 0.01 N aqueous hydrochloric acid and then water. The ethereal layer was then dried over magnesium sulfate and 3Å molecular sieves. Evaporation of the solvent yielded 30 mg (30%) of a colorless solid, mp. 164.5-165.2°. A 50:50 mixture (by weight) of the product with IIa, mp. 151.2-151.7°, resulted in a melting point depression, mp. 147.4-156.0°.

NMR (CDCl<sub>3</sub>): δ 0.63 (C<sub>18</sub>-CH<sub>3</sub>), 0.88 (C<sub>19</sub>-CH<sub>3</sub>), 2.60 (CH-C=O), no -CO<sub>2</sub>H (in IIa δ 11.4); no vinyl proton (in IIa δ 5.37); IR (KBr): 1765 cm<sup>-1</sup> (lactone), no peak at 1700 cm<sup>-1</sup> (C=O in IIa); MS (70 eV, 100°): m/e (relative intensity) 414 (M<sup>+</sup>, 61.4); 386 ((M-CO)<sup>+</sup>, 24.5); 370 ((M-CO<sub>2</sub>)<sup>+</sup>, 26.8); 329 (4.86); 301 ((M-C<sub>8</sub>H<sub>17</sub>)<sup>+</sup>, 29.1);<sup>6</sup> 288 (50.0); 274 (62.3); 260 ((M-C<sub>11</sub>H<sub>22</sub>)<sup>+</sup>, 79.1);<sup>6</sup> 259 ((M-C<sub>11</sub>H<sub>23</sub>)<sup>+</sup>, 100).<sup>6</sup>

Anal. Calcd. for C<sub>28</sub>H<sub>46</sub>O<sub>2</sub>: C, 81.10; H, 11.18.

Found: C, 81.18; H, 11.38.

Procedure B (from IIb).- Using diazomethane generated from EXR-101,<sup>7</sup> the 3α-acid (IIa) was converted to its methyl ester (IIb).

NMR(CDCl<sub>3</sub>): δ 2.48 (CH-C=O), 3.65 (-CO<sub>2</sub>CH<sub>3</sub>), 5.36 (vinyl H); IR(KBr): 1728 cm<sup>-1</sup>.

Methyl 3α-cholestene-Δ<sup>5</sup>-carboxylate (IIb) (100 mg) when

subjected to the same conditions as those described in procedure A, yielded 25 mg (26%) of a colorless solid, mp. 164.2-165.3<sup>o</sup>, which when mixed with an equal weight of IIa, resulted in a melting point depression, mp. 147.0-157.8<sup>o</sup>. When the product was mixed with the product in A, there was no mp. depression, mp. 164.2-165.8<sup>o</sup>.

NMR (CDCl<sub>3</sub>): no -CO<sub>2</sub>H, no vinyl proton; IR(KBr) 1765 cm<sup>-1</sup> (lactone), no peak at 1700 cm<sup>-1</sup> (-CO<sub>2</sub>H).

## REFERENCES

1. E. J. Corey and R. A. Sneen, *J. Am. Chem. Soc.*, 75, 6234 (1953), concluded that the failure to observe (IR) or isolate I from a mixture of the epimer acid of I in hydrogen chloride (chloroform) constituted strong evidence for the epimer being assigned the 3 $\beta$  (equatorial)-CO<sub>2</sub>H structure.
2. P. Wintersdorf, "Acidic Hydrolysis of Some Steroid Esters", MS Thesis, San Diego State University, San Diego, California, p. 22, 1968.
3. G. Roberts, C. W. Shoppee and R. J. Stephenson, *J. Chem. Soc.*, 2705 (1954).
4. C. F. Gelger, 312 E. Yale St., Ontario, CA.
5. Use of the large excess of NaOH probably led to lactone (I) ring opening and a lowered yield; neutralization to pH 7 would be better (We thank a referee).
6. H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds", p. 63, Holden-Day, San Francisco, 1967.
7. R. S. Manson, "Advanced Organic Synthesis", Vol. 1, p. 58, Academic Press, New York, 1971.