



the carbon and oxygen positions with isotropic thermal parameters is continuing. The R factor is 11.8% at the present time. The data revealed the presence of four crystallographically independent molecules of 3c in the cell.7 ORTEP views (50% probability thermal ellipsoids) of molecule 2 are seen in Figure 1. The structure of 3c is unequivocally  $5\alpha$ ,  $17\alpha$ -cholest-14-en- $3\beta$ -ol *p*-bromobénzoate. Molecules 1, 2, and 4 have the same D ring conformation,  $17\beta$ envelope, and similar side chain orientation; C-21 is anti to C-13 and gauche to C-16. In molecule 3 the D-ring conformation appears to be a  $17\alpha$  envelope and C-21 is gauche to C-13 and C-16. The end of the cholestane side chain, C-25, C-26, C-27, is probably disordered in at least two of the molecules. Other interesting conformational details which vary in the four molecules will be discussed in a future paper.

The saturated derivative 4 obtained by hydrogenation of 3 could have either the  $14\alpha$  or  $14\beta$  stereochemistry. From <sup>13</sup>C NMR studies<sup>4</sup> of 4c and 4d, it was tentatively concluded that 4 is  $5\alpha.14\beta.17\alpha$ -cholestan- $3\beta$ -ol.

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Supplementary Material Available. Tables of <sup>13</sup>C chemical shifts and bond distances and angles will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105  $\times$  148 mm, 24 $\times$  reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for \$4.50 for photocopy or \$2.50 for microfiche, referring to code number JOC-75-2005.

## **References and Notes**

- (1) Professor A. Fiecchi and his associates at the University of Milano have obtained similar results. It was agreed to publish the results of both groups simultaneously. (2) J. W. Cornforth, I. Y. Gore, and G. Popjak. *Biochem. J.*, **65**, 94 (1957).
- These authors have carried out the referred to transformation on the  $\Delta^{8(14)}$  benzoate. We have carried out the reactions described in this communication on both  $\Delta^{8(14)}$  acetate and the benzoate. In both instances analogous products were obtained which were interrelated as the free C-3 alcohol. At present we report the results for the acetate.
- (3) All new compounds were fully characterized. <sup>1</sup>H NMR spectra were re-corded on a Varian DA-60 instrument. <sup>13</sup>C NMR spectra were obtained on a Varian HA 100-15 instrument equipped with a Varian time-averaging computer (C-1024) and were recorded at 25.1 MHz. Mass spectra were obtained on a Du Pont 21-491 instrument.

Communications

- (4) A table of <sup>13</sup>C chemical shifts of these compounds is published in the mi-
- crofilm edition of the journal immediately following these pages.
  C. Djerassi, *Pure Appl. Chem.*, 21, 205 (1970).
  T. A. Wittstruck and K. I. Williams, *J. Org. Chem.*, 38, 1542 (1973). (6)
- (7) A table of bond distances and angles averaged over the four molecules is published in the microfilm edition of the journal immediately following these pages.
- (a) Worcester Foundation for Experimental Biology, Shrewsbury, Mass. 01545. (b) Medical Foundation of Buffalo Research Laboratorles, Buffalo, (8)N.Y. 14203. (c) Extracted in part from the Ph.D. Thesis of J. P. Moreau to be submitted to the University of Orleans, France.

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## A Ready Synthesis of $17\alpha$ Steroids<sup>1,2</sup>

Summary: Reaction of sterol acetates with a  $\Delta^7$ ,  $\Delta^{8(14)}$ , and  $\Delta^{14}$  double bond with hydrogen chloride yields  $3\beta$ -acetyloxy-14-chloro- $5\alpha$ , 14 $\beta$ , 17 $\alpha$ -cholestane (structure determined by X-ray analysis), which is easily dehydrohalogenated to  $3\beta$ -acetyloxy- $5\alpha$ ,  $17\alpha$ -cholest-14-ene.

Sir: Anhydrous hydrogen chloride in chloroform has been described to promote the isomerization of  $\Delta^7$ ,  $\Delta^8$ , and  $\Delta^{8(14)}$ double bonds to the 14 position in sterols.<sup>3,4</sup> Compound 1a (mp 104-106°) was obtained as the single reaction product by bubbling hydrogen chloride for 3 hr at  $-60^{\circ}$  in a 20-25 mM solution of  $3\beta$ -acetyloxy- $5\alpha$ -cholest-7-ene (2) in diethyl ether. The <sup>1</sup>H NMR spectrum showed signals at  $\delta$ 





Figure 1. ORTEP plot of  $3\beta$ -acetoxy-14-chloro- $5\alpha$ ,  $14\beta$ ,  $17\alpha$ -cholestane.

0.81 (C<sub>19</sub> CH<sub>3</sub>, s) and 1.18 (C<sub>18</sub> CH<sub>3</sub>, s). The molecular ion was absent in the mass spectrum which differed from that of 3a only in the relative intensity of fragmentation peaks. By X-ray diffraction analysis the compound was shown to give orthorombic crystals with cell dimensions: a = 34.148(10), b = 12.538 (2), c = 6.641 (2) Å; space group  $P2_12_12_1$ , Z = 4. A total of 1371 reflections was measured up to  $\vartheta$  = 45°. The structure was solved by direct methods employing the program MULTAN.<sup>5</sup> The final R index was 0.091 for the 1125 reflections with Int. >  $2\sigma$  Int. The crystal structure analysis showed that the examined compound is  $3\beta$ -acetyloxy-14-chloro- $5\alpha$ ,  $14\beta$ ,  $17\alpha$ -cholestane (1a). The ORTEP plot of the molecule is reported in Figure 1.6

Formation of 1b in the reaction of  $3\beta$ -benzovloxy- $5\alpha$ cholest-8(14)-ene (4b) with hydrogen chloride has been reported by Cornforth et al.<sup>4</sup> According to these authors the compound is transformed into  $3\beta$ -benzoyloxy- $5\alpha$ -cholest-14-ene (3b) by shaking the reaction mixture with a saturated solution of sodium hydrogen carbonate. Treatment of 1a under these conditions failed to transform the compound into 3a, whereas 1a with excess triethylamine in methanol at 50° gave the acetate 3c, which showed <sup>1</sup>H NMR signals at  $\delta$  0.87 (C<sub>19</sub> CH<sub>3</sub>, s), 1.09 (C<sub>18</sub> CH<sub>3</sub>, s), and 5.08 (H<sub>15</sub>, m). The mass spectrum showed differences only in the relative intensity of the peaks when compared with that of compound 3a. Compound 3c failed to crystallize but a crystalline  $3\beta$ -p-bromobenzoyloxy derivative (3d, mp 101–102°) was obtained (orthorombic with cell dimensions: a = 22.15, b = 51.87, c = 11.05 Å; space group  $P2_12_12_1; Z = 16$ ; automatic diffractometer data).<sup>7</sup> From the above reported spectral data, the structure of  $3\beta$ -acetyloxy- $5\alpha$ ,  $17\alpha$ -cholest-14ene was considered the most probable for compound 3c. To confirm this hypothesis, reductive ozonolysis of compound 3c was performed. The oily ketoaldehyde 5a was obtained from the reaction. It showed <sup>1</sup>H NMR signals at  $\delta$  0.88 (C<sub>19</sub> CH<sub>3</sub>, s), 1.2 (C<sub>18</sub> CH<sub>3</sub>, s), and 9.67 (H<sub>15</sub>, t,  $J \sim 1.5$  H). The mass spectrum of 5a showed an intense peak at m/e 292 corresponding to the loss of a  $C_{11}H_{20}O$  fragment from the molecular ion. The structure either of aldehyde 6 or of an isomer of this aldehyde might be assigned to this fragment, since 4,8-dimethylnon-2-en-1-al (6), isolated as the semicarbazone, was obtained by pyrolysis of 5a. On the other hand pyrolysis of 5b was described by Cornforth et al.<sup>4</sup> to give 6, thus confirming the presence of a  $\Delta^{14}$  double bond in 3c.

Acetate 1a was obtained with hydrogen chloride at low temperature also from 3a, 3c, and 4a. On the basis of these experimental evidences, the mechanism shown in Scheme I may be hypothesized for this reaction. Dilution and low temperature seem to promote the formation of 3a instead of 1c which is obtained under the conditions reported by Cornforth et al.<sup>4</sup> Trans addition of HCl to the  $\Delta^{14}$  double bond starting with the attack of a proton at carbon 15 from the less hindered  $\alpha$  side of the molecule would yield  $3\beta$ acetyloxy-14-chloro- $5\alpha$ , 14 $\beta$ -cholestane (a). From the molecular model it is apparent that the  $14\beta$ -Cl,  $13\beta$ -CH<sub>3</sub>, and  $17\beta$  side chains strongly interact and that these interactions can be avoided by elimination of chloride ion, followed by ring C contraction and formation of the spiranic olefin b with loss of the  $17\alpha$  hydrogen.<sup>8</sup> Reaction of the spi-



ranic olefin b with hydrogen chloride formally reverses the rearrangement starting from the attack of a proton at  $17\beta$ position and with the final introduction of chloride ion at position  $14\beta$ .<sup>9</sup>

Supplementary Material Available. A table of atomic coordinates and equivalent temperature factors will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105  $\times$  148 mm, 24 $\times$  reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for \$4.00 for photocopy or \$2.50 for microfiche, referring to code number JOC-75-2006.

## **References and Notes**

- (1) This investigation was supported by the Italian National Research Council.
- (2) Dr. E. Caspi and his associates at the Worcester Foundation have obtained similar results. It was agreed to publish the results of both groups simultaneously
- (3) L. F. Fleser and M. Fleser, "Steroids", Reinhold, New York, N.Y., 1959, pp 113, 260, 354, 400, and references cited therein. J. W. Cornforth, I. Y. Gore, and G. Popjak. *Biochem. J.*, **65**, 84 (1957).
- (5) G. Germain, P. Main, and M. M. Woolfson, Acta Crystallogr., A27, 368 (1971)
- (6) The reflections were measured with a Philips PW 1100 automatic diffractometer (Cu K $\alpha$  radiation monochromatized with a flat graphite crystal;  $\vartheta - 2\vartheta$  scan mode; scan rate 0.03°/min; scan width 1.2°  $\vartheta$ ). The positional and anisotropic thermal parameters of nonhydrogen atoms were refined by full matrix least-squares calculations. The hydrogen atoms could not be discerned on the difference Fourier map; so they were placed at their theoretically expected positions and held fixed during refinement. Bond distances and angles are all within the range of the expected values except three C-C distances involving atoms belonging to the side chain in 17; these atoms exhibit very high thermal vibrations. The average of the absolute values of the torsion angles inside rings A, B, and C are 58.1, 58.4, and 54.2°, respectively. The D ring is a slightly distorted  $13\beta$ -envelope conformation. The angle between the least-squares plane of rings C and D is 68°. The only intermolecular distance less than 3.6 Å occurs between C4 and O28 and is 3.41 Å.
- When the X-ray analysis was in progress Dr. Caspi informed us that he and his associates had already determined the structure of this compound.
- A transposition of this type has been reported by A. Lardon and T. Reichstein, *Helv. Chim. Acta*, **45**, 943 (1962). It is caused by SoCl<sub>2</sub> in pyridine on methyl  $5\beta$ ,  $14\beta$ -androstane- $3\beta$ , 14-dihydroxy-15-oxo-17 $\beta$ -carboxylate and similar compounds.
- (9)A carbonium ion formed from 3a or directly from 4a at C14 seems unlikely since there is no conformation of the molecule in which the C12-C13 bond is aligned with the vacant p orbital at C<sub>14</sub> as it appears from molecular models. This assumption is supported by the evidence that the transposition of the  $10\beta$ -methyl group pf  $5\alpha$ -cholestane- $4\alpha$ ,5-diol- $4\alpha$ -acetate occurs owing to the alignment of the C10-C19 bond with the vacant p orbital at Cs. Čf. E. T. J. Bathurst, J. M. Coxon, and M. P. Hartshorn, Aust. J. Chem., 27, 1505 (1974).

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