

# Thermal Rearrangement of a Ketovinylcyclobutene to a Ketobicyclo[3.1.0.]hexene<sup>1</sup>

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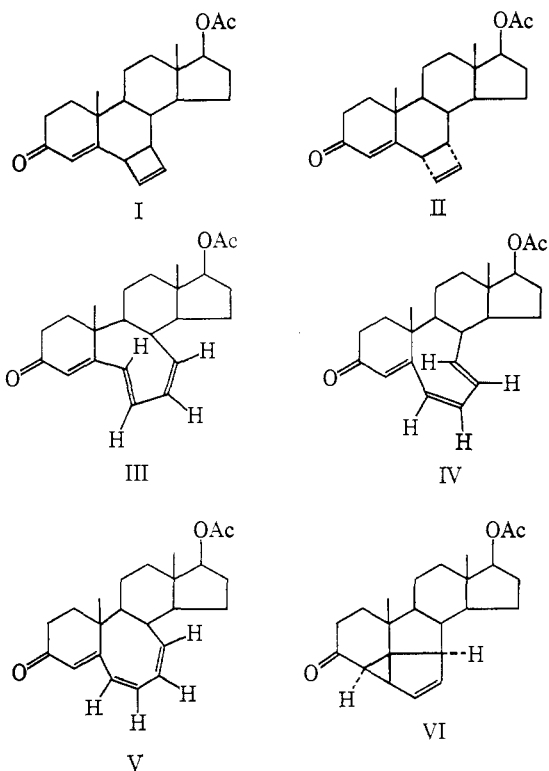
Contribution from the Institute of Steroid Chemistry, Syntex Research, Palo Alto, California. Received February 7, 1968

**Abstract:** The isomeric 6 $\alpha$ ,7 $\alpha$ - and 6 $\beta$ ,7 $\beta$ -vinylettestosterone acetates I and II are converted into the same compound by heating above 150°. The chemical and physical properties of the product indicate that it has the unusual structure VI, which incorporates a bicyclo[3.1.0.]hexene system.

The thermal isomerization of variously substituted cyclobutenes to the corresponding butadienes is well established, and has been found to proceed stereospecifically.<sup>3</sup> The geometry of the product can be predicted from orbital symmetry considerations.<sup>4</sup>

The preparation of the epimeric 6,7-vinylettestosterone acetates I and II<sup>5</sup> afforded an opportunity to study the pyrolytic behavior of these novel cyclobutene compounds.

According to the Woodward-Hoffmann rules<sup>4</sup> concerted pyrolytic opening of I and II should give III or IV. However, it was also anticipated that the product could be V (see Discussion). In practice, none of these compounds was formed; pyrolysis of either I or II at 210–215° gave a single product which has the unusual



(1) Contribution CCCXXXIX from the Syntex Institute of Steroid Chemistry; for part CCCXXXVIII, see I. Vlatts, I. T. Harrison, L. Tökés, J. H. Fried, and A. D. Cross, submitted for publication.

(2) Syntex Postdoctoral Fellow, 1965–1966.

(3) See, for example, E. Vogel, *Ann.*, 615, 14 (1958); R. Criegee and K. Noll, *ibid.*, 627, 1 (1959), and W. Adam, *Chem. Ber.*, 87, 1811 (1964).

(4) (a) R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, 87, 395 (1965); (b) H. C. Longuet-Higgins and E. W. Abrahamson, *ibid.*, 87, 2046 (1965).

(5) P. H. Nelson, J. W. Murphy, J. A. Edwards, and J. H. Fried, *ibid.*, 90, 1307 (1968).

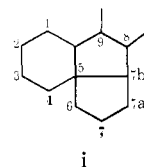
structure VI. The constitution of VI was deduced from its spectral properties and from a series of chemical transformations.

The mass spectrum of the pyrolysis product indicated that it was a result of rearrangement, since the base peak,  $m/e$  354, corresponded to the molecular ion of VI. The fragmentation pattern of VI will be discussed later.

The olefinic region of the nmr spectrum of the pyrolysis product is shown in Figure 1. The assignments of the signals and of the coupling constants rest on the expectation that the allylic coupling constant,  $J_{6,7a}$ ,<sup>6</sup> would be considerably smaller than the allylic coupling constant  $J_{7,7b}$ . This analysis was suggested by inspection of a Dreiding model of VI which shows the relevant dihedral angles  $C_6H-C_{7a}H$  and  $C_7H-C_{7b}H$  to be 30 and 60°, respectively.<sup>7</sup> Since the smaller of the two angles would be expected to lead to the smaller allylic coupling constant,<sup>8</sup> the assignments were made as shown in Figure 1. Spin-spin decoupling experiments clarified the coupling patterns and also allowed the approximate location of the resonances due to  $H_6$  and  $H_{7b}$ .<sup>9</sup>

The mass spectrum of VI shows, in addition to the molecular ion at  $m/e$  354 (intensity = 100%),<sup>10</sup> an ion at  $m/e$  297 (43%) corresponding to a loss of  $C_3H_5O$  (carbons 1, 2, and 3 plus a hydrogen atom). The presence of a substituent at  $C_4$  is suggested by the absence of  $M - 71$  and  $M - 72$  ions, since unsubstituted steroidal 3-ketones readily undergo this fragmentation (loss of carbons 1, 2, 3, and 4 plus one or two hydrogen atoms).<sup>11</sup> In addition, ions corresponding to losses

(6) Compounds are numbered as in i according to IUPAC rule S-7.3 (Nomenclature of Organic Compounds, Butterworth Scientific Publications, London, 1957, p 82).



(7) Bond angles are measured to the nearest 5°.

(8) T. A. Wittstruck, S. K. Malhotra, and H. J. Ringold, *J. Amer. Chem. Soc.*, 85, 1699 (1963); D. J. Collins, J. J. Hobbs, and S. Sternhell, *Aust. J. Chem.*, 16, 1030 (1963).

(9) See Experimental Section.

(10) Mass spectra were recorded from  $m/e$  40 to the molecular ion position.

(11) R. H. Shapiro, D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, 86, 2837 (1964); the presence of a substituent at  $C_3$  should not prevent fragmentation to give  $M - 71$  and  $M - 72$  ions, since these authors showed that transfer of the 5 $\alpha$ -H accounts for only a small proportion of the total migration of hydrogen. This conclusion is supported by the mass spectrum of the tetrahydro compound VII which is described later.

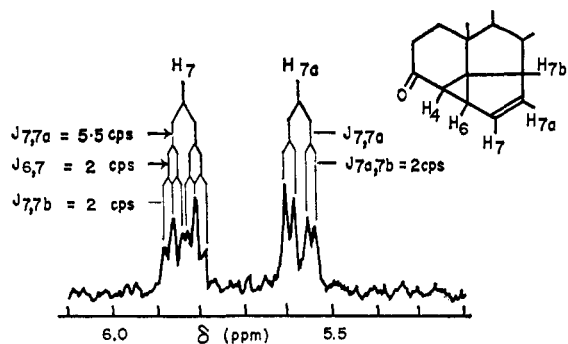
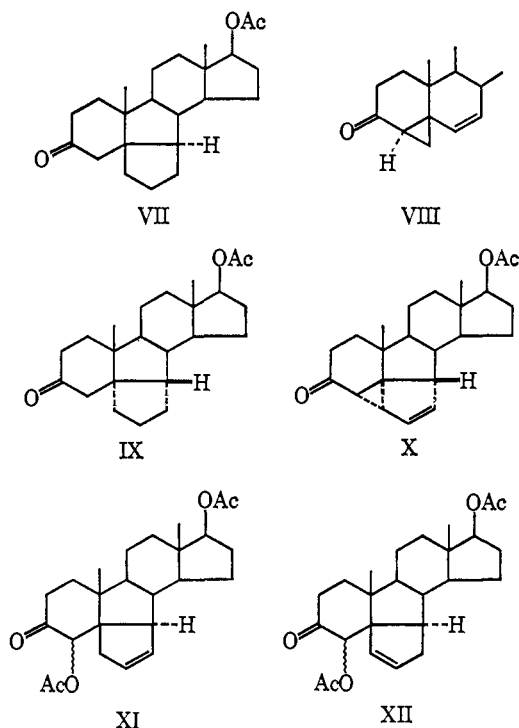


Figure 1. Low-field nmr spectrum of VI.

of  $\text{CH}_3$ ,  $\text{CH}_3\text{CO}_2\text{H}$ ,  $(\text{CH}_3 + \text{CH}_3\text{CO}_2\text{H})$ , and  $(\text{CH}_3\text{CO}_2\text{H} + \text{CH}_2\text{CO})$  were present, the latter ( $m/e$  212) having a relative intensity of 27%.

The presence of a conjugated system in VI was indicated by its uv spectrum ( $\lambda_{\text{max}}$  232  $m\mu$  ( $\epsilon$  7050)). The values are very similar to those of the related chromophore VIII ( $\lambda_{\text{max}}$  231  $m\mu$  ( $\epsilon$  5750)).<sup>12</sup>

Catalytic hydrogenation of VI yielded a tetrahydro compound VII. The negative Cotton effect ( $a = -61$ ) in the ORD spectrum of this compound indicates the  $\beta$  orientation of the extra five-membered ring as in VII, since a model shows that carbons 5, 6, 7, 7a, and 7b lie in a negative octant. The original pyrolysis product must therefore be VI rather than the epimer X which could, at least formally, have been produced from a hypothetical trienone intermediate III, IV, or V.



The mass spectrum of VII showed a strong molecular ion at  $m/e$  358 (50%). Fragments were also present corresponding to losses of  $\text{CH}_3\text{CO}_2\text{H}$  ( $m/e$  298, 26%) and, more significantly, of 71 and 72 mass units. The latter fragments are caused by loss of the four ring A carbon atoms, and, as discussed above, are characteristic of steroidal 3-ketones unsubstituted at  $\text{C}_4$ .

(12) W. G. Dauben, private communication.

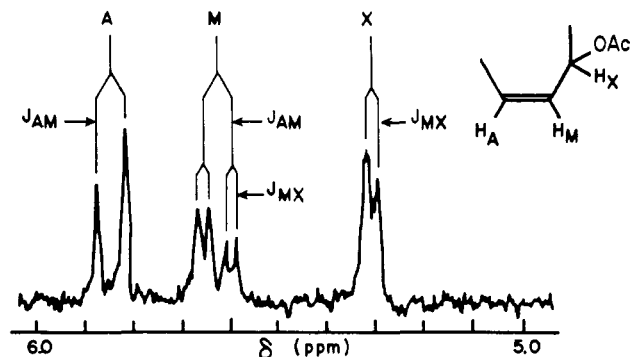


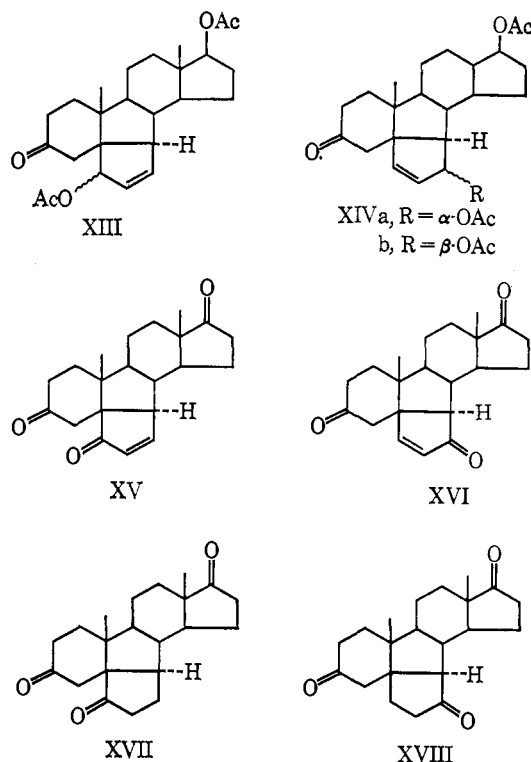
Figure 2. Low-field nmr spectrum of acetolysis product XIII or XIV.

Acetolysis of VI (refluxing acetic acid containing a trace of *p*-toluenesulfonic acid) gave a crystalline compound in high yield. The mass spectrum showed a weak molecular ion at  $m/e$  414 (4%) corresponding to  $(\text{VI} + \text{CH}_3\text{CO}_2\text{H})$ . The only other fragments of significant intensity corresponded to  $\text{M} - 42$  (3%) and  $\text{M} - 43$  (9%).<sup>13</sup>

Of the four possible acetolysis products, XI, XII, XIII, and XIV, the first two can be eliminated by examination of the nmr spectrum, since the singlet which would have been ascribable to the 4-H in XI and XII is not present.

The spectrum showed three low-field protons in a slightly perturbed AMX pattern (see Figure 2) which could be produced by either XIII or XIV if it is assumed that  $J_{7a,7b}$  is small ( $<0.5$  cps).

In order to distinguish between the two possible structures, the acetolysis product XIII or XIV was converted by hydrolysis and oxidation to an  $\alpha,\beta$ -unsaturated ketone XV or XVI. The olefinic protons of this com-

(13) The base peak was at  $m/e$  43.

pond formed a sharp AB quartet in the nmr spectrum. The absence of any additional coupling tends to favor structure XVI. This conclusion was supported by the positions of the 19-H resonances of the compounds shown in Table I.

Table I. 19-H Resonances

Compound	$\delta$ , ppm
Tetrahydro compound VII	1.08
Hydrogenated enone XVII or XVIII <sup>a</sup>	1.07
Acetolysis product XIII or XIV	0.85
Enone XV or XVI	0.93

<sup>a</sup> Produced by catalytic hydrogenation of the enone XV or XVI

The significant upfield shift exhibited by the latter two compounds can be ascribed to the presence of the carbon-carbon double bond in the acetolysis product. Dreiding models of these compounds show that the shielding zone of this double bond<sup>14</sup> will only encompass the 19-H if it is in the 6,7 position as in XIV and XVI.

Finally, the possible structures XVII and XVIII for the hydrogenated enone were unambiguously distinguished by deuterium exchange, which led to the incorporation of nine deuterium atoms. Since XVII has only eight replaceable hydrogens whereas XVIII has nine, the latter structure must be correct.

These results also establish the structure of the initial acetolysis product as XIV. The orientation of the acetoxy group can be predicted with reasonable certainty to be  $\alpha$  as in XIVa, since the dihedral angle between the noncoupling hydrogens 7a and 7b in this structure is approximately 120°, whereas in the  $\beta$ -oriented acetate XIVb it is near 0°. It is generally accepted that a 120° dihedral angle is more likely to lead to zero coupling constant than is an angle of 0°.

### Mechanism of Formation of VI

Any mechanistic proposal advanced for the formation of VI must be consistent with the following observations. (a) The transformations are relatively facile, proceeding slowly at 150° and readily at 210°. (b) An intermediate product was not detected either by thin layer chromatographic monitoring of the reactions, or by work-up of incomplete reactions. (c) Both I and II yielded VI. Carbon 7b must therefore assume a planar configuration during the reaction.

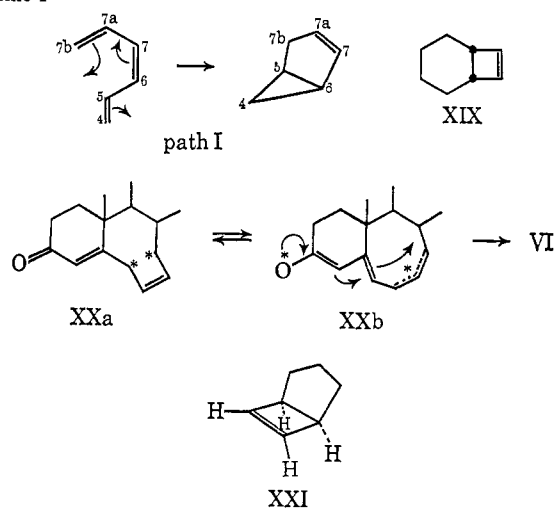
The latter condition could be met by opening of the cyclobutene ring to give a cyclooctadiene compound. Subsequent internal Diels-Alder reaction (path I of Scheme I)<sup>15</sup> would then give VI.

The preferred pathway for concerted thermal fission of cyclobutenes is by a conrotatory process. Thus I or II would give one of the *cis,trans*-cycloocta-1,3-diene compounds III and IV. Considerations of orbital symmetry indicate IV to be the more likely intermediate for the formation of VI since it can undergo an energetically favorable *trans,trans* internal Diels-Alder reaction, whereas transformation of III into VI would

(14) J. W. ApSimon, W. G. Craig, P. V. Demarco, D. W. Mathieson, L. Saunders, and W. B. Whalley, *Tetrahedron*, **23**, 2357 (1967).

(15) An analogous transformation has recently been described: W. Merck and R. Pettit, *J. Amer. Chem. Soc.*, **89**, 4787 (1967).

Scheme I



require a *cis,trans* Diels-Alder reaction in which orbital symmetry is not conserved.<sup>16,17</sup>

Although *cis,trans*-cycloocta-1,3-diene has been isolated,<sup>18</sup> it is converted on heating to 80° into the conrotatory cyclization product *cis*-bicyclo[4.2.0]octene.<sup>19</sup> The additional steric strain which would be imposed by the presence of an exocyclic double bond and by the fusion of the steroidal A and C rings would further destabilize III and IV relative to the starting cyclobutenes. Dreiding models fully support this conclusion. However, it should be noted that the sequence I or II  $\rightarrow$  IV  $\rightarrow$  VI appears feasible when the flexible Prentice-Hall models are used.<sup>17,20</sup>

Nevertheless, the ease with which I and II undergo thermal isomerization is in striking contrast to the reluctance of XIX to undergo a similar process. XIX is stable below 250°, and above this temperature is isomerized into *cis,cis*-cycloocta-1,3-diene. This observation has been ascribed to steric hindrance of the symmetry allowed conrotatory pathway.<sup>21</sup>

This disparity suggests that the isomerization of I and II may proceed by an initial fission of the 6-7 bond to give the resonance-stabilized diradical XX. The distance between C<sub>5</sub> and C<sub>7b</sub> in XXb is only 2.8 Å and, more significantly, considerable  $\pi$  overlap can occur between these centers. Electron reorganization to give VI, therefore, seems quite feasible.

In order that XX can be an intermediate in both pyrolyses, it must be sufficiently long lived for it to be able to adopt the conformation which would cyclize to VI rather than X. Models suggest only one stable conformation for XXb and further that this would definitely cyclize to VI and not to X.

The theoretically possible concerted disrotatory ring opening to give the less strained *cis,cis*-cyclooctadiene intermediate V would be expected to proceed at appreciably higher temperatures than were necessary for

(16) R. Hoffmann and R. B. Woodward, *ibid.*, **87**, 2046, 4388 (1965); *Accounts Chem. Res.*, **1**, 17 (1968).

(17) We are grateful to a referee for drawing this point to our attention.

(18) A. C. Cope and C. L. Bumgardner, *J. Amer. Chem. Soc.*, **78**, 2812 (1956).

(19) K. M. Shumate, P. N. Neumann, and G. J. Fonken, *ibid.*, **87**, 3966 (1965).

(20) Framework Molecular Models, Prentice-Hall Inc., Englewood Cliffs, N. J.

(21) R. Criegee, D. Seebach, R. E. Winter, B. Börretzen, and H. A. Brune, *Chem. Ber.*, **98**, 2339 (1965).

the production of VI. Thus XXI, which cannot undergo conrotatory ring opening, is isomerized to *cis,cis*-dimethylcycloheptadiene only above 400°. <sup>22</sup>

Furthermore, even if V were formed, the subsequent transformation into VI would apparently be a very high-energy process. This conclusion is based on orbital symmetry considerations<sup>23</sup> and on an examination of Dreiding models which show that the distance between C<sub>5</sub> and C<sub>7b</sub>, which must be joined in the final product, is *ca.* 3 Å, and that  $\pi$  orbital overlap does not occur. The rigidity of V precludes any significant change in these parameters due to skeletal vibrations. <sup>24</sup>

### Acetolysis of VI

The acetolysis of VI affords XIVa exclusively; no additional products were detected by tlc. The absence of a 4-acetoxy product suggests that protonation occurs preferentially at the 3-ketone rather than the cyclopropane ring. The orientation of the acetoxy group is that which would be obtained in an SN2' reaction (entering and leaving groups in a *cis* orientation). However, the experimental data available are insufficient to exclude nonconcerted mechanisms.

### Experimental Section<sup>25</sup>

**Pyrolysis of 17 $\beta$ -Acetoxy-6,7-vinylenandrost-4-en-3-ones (I and II).** The steroid (150 mg) was heated at 215° for 15 min under nitrogen. The pale yellow product was decolorized by percolating a solution in ethyl acetate-hexane through *ca.* 0.5 g of silica gel. The product was crystallized from hexane to give 17 $\beta$ -acetoxy-B-bishomo-4 $\beta$ ,6 $\alpha$ -cyclo-5 $\alpha$ ,7 $\beta$  $\alpha$ -cycloandrosta-4,7-dien-3-one (VI, 120 mg, 80%): mp 172–173°; ORD [ $\Phi$ ]<sub>600</sub> +272°, [ $\Phi$ ]<sub>347</sub>  $\pm$ 0°, [ $\Phi$ ]<sub>323</sub> -3530°, [ $\Phi$ ]<sub>309</sub>  $\pm$ 0°, [ $\Phi$ ]<sub>247</sub> +63,700°, [ $\Phi$ ]<sub>233</sub>  $\pm$ 0°, [ $\Phi$ ]<sub>215</sub> -10,800°;  $\lambda_{\max}$  232 m $\mu$  ( $\epsilon$  7050);  $\nu_{\max}$  1730, 1690, 1570 cm<sup>-1</sup>; nmr 0.82 (18-H), 0.96 (19-H), 2.02 (17 $\beta$ -acetoxy-H), 4.5–4.7 (17 $\alpha$ -H), and 5.5–5.9 ppm (two-proton multiplet; see text). Double resonance experiments indicated that H<sub>6</sub> and H<sub>7b</sub> resonated at *ca.* 1.37 and *ca.* 1.56 ppm, respectively; mass spectrum 354 (M<sup>+</sup>, 100%), 339 (6%), 326 (1%), 321 (1%), 312 (6%), 297 (43%), 294 (4%), 279 (25%), 252 (28%), and 237 (59%). *Anal.* Calcd for C<sub>23</sub>H<sub>30</sub>O<sub>3</sub>: C, 77.93; H, 8.53. Found: C, 77.68; H, 8.40.

(22) R. Criegee and H. Furrer, *Chem. Ber.*, **97**, 2949 (1964).

(23) Conversion of V to VI would require an unfavorable *cis,trans* internal Diels-Alder reaction; see ref 16.

(24) We wish to thank Dr. J. I. Brauman, Department of Chemistry, Stanford University, for useful discussions of some aspects of the mechanism of formation of VI.

(25) Melting points are uncorrected and were taken on a Fisher-Johns apparatus. Optical rotations were measured at 27° in dioxane solution on an O. C. Rudolph and Sons, Model 80 polarimeter. Ultraviolet spectra were measured in ethanol on a Cary Model 14 spectrometer. Infrared spectra were measured as Nujol mulls on a Perkin-Elmer Model 137 spectrophotometer. Nmr spectra were recorded on Varian HA 100 and A 60 spectrometers using deuteriochloroform as solvent. Double-resonance experiments were carried out using a Hewlett-Packard 200 AB audio oscillator. Chemical shifts are recorded in parts per million (ppm) relative to TMS on the  $\delta$  scale to the nearest 0.01 ppm. Coupling constants are reported in cycles per second (cps) to the nearest 0.5 cps. We wish to thank Miss J. Tremble for assistance with these measurements. Mass spectra were measured on an Atlas CH-4 spectrometer equipped with TO-4 ion source. The ionizing energy was maintained at 70 eV and the ionizing current at 10  $\mu$ A. We wish to thank Mr. J. Smith for assistance with these measurements. Optical rotatory dispersion (ORD) curves were measured in dioxane on a Jasco ORD/UV-5 spectrometer. Sufficient values are quoted to allow a rough curve to be plotted. Analytical tlc plates with a thickness of 0.25-mm silica gel GF<sub>254</sub> (E. Merck A. G., Darmstadt) and preparative tlc plates with thicknesses of 0.25-mm silica gel GF<sub>254</sub> and 1.3-mm silica gel HF<sub>254</sub> were used.

**Catalytic Hydrogenation of VI.** VI (25 mg) was hydrogenated in ethanol (3 ml) over 5% palladium on carbon (5 mg) for 30 min. The catalyst was removed by filtration, the solution evaporated, and the residue crystallized from hexane to give a quantitative yield of 17 $\beta$ -acetoxy-B-bishomo-5 $\alpha$ ,7 $\beta$  $\alpha$ -cycloandrostan-3-one (VII): mp 130–133°; [ $\alpha$ ]<sub>D</sub> -23°; ORD [ $\Phi$ ]<sub>600</sub> +70°, [ $\Phi$ ]<sub>399</sub> -81°, [ $\Phi$ ]<sub>450</sub> -150°, [ $\Phi$ ]<sub>350</sub> -795°, [ $\Phi$ ]<sub>322</sub> -3030°, [ $\Phi$ ]<sub>316</sub> -2180°, [ $\Phi$ ]<sub>310</sub> -2730°, [ $\Phi$ ]<sub>303</sub> -500°, [ $\Phi$ ]<sub>298</sub>  $\pm$ 0°, [ $\Phi$ ]<sub>292</sub> +1560°, [ $\Phi$ ]<sub>277</sub> +3060°, [ $\Phi$ ]<sub>210</sub> +1110°;  $\nu_{\max}$  1735, 1725 cm<sup>-1</sup>; nmr 0.78 (18-H), 1.08 (19-H), 2.02 (17 $\beta$ -acetoxy-H), and 4.3–4.6 ppm (17 $\alpha$ -H); mass spectrum 358 (M<sup>+</sup>, 46%) and 298 (22%). *Anal.* Calcd for C<sub>23</sub>H<sub>34</sub>O<sub>3</sub>: C, 77.05; H, 9.56. Found: C, 76.93; H, 9.70.

**Acetolysis of VI.** VI (50 mg) was refluxed in a solution of *p*-toluenesulfonic acid (1 mg) in acetic acid (5 ml) for 15 min under nitrogen. The cooled solution was poured into ethyl acetate and washed (1% sodium bicarbonate, water), dried, and evaporated. The pale yellow residue was recrystallized from ethyl acetate-hexane to give 7 $\alpha$ ,17 $\beta$ -diacetoxy-B-bishomo-5 $\alpha$ ,7 $\beta$  $\alpha$ -cycloandrosta-6-en-3-one (XIVa, 33 mg, 55%): mp 122–124°; [ $\alpha$ ]<sub>D</sub> -93°; ORD [ $\Phi$ ]<sub>600</sub> -427°, [ $\Phi$ ]<sub>389</sub> -383°, [ $\Phi$ ]<sub>321</sub> -4820°, [ $\Phi$ ]<sub>315</sub> -4150°, [ $\Phi$ ]<sub>310</sub> -4990°, [ $\Phi$ ]<sub>304</sub> -1880°, [ $\Phi$ ]<sub>300</sub> -3390°, [ $\Phi$ ]<sub>294</sub> -1870°, [ $\Phi$ ]<sub>290</sub> -1950°, [ $\Phi$ ]<sub>235</sub> -1370°, [ $\Phi$ ]<sub>231</sub> -1510°, [ $\Phi$ ]<sub>260</sub> -3880°, [ $\Phi$ ]<sub>214</sub> -31600°;  $\nu_{\max}$  1730, 1705 cm<sup>-1</sup> (shoulder); nmr 0.76 (18-H), 0.85 (19-H), 2.00 and 2.02 (two acetoxy methyls), 2.45 (two proton singlet, 4-H), 4.4–4.9 (17 $\alpha$ -H), 5.39 (doublet, *J* = 2.5 cps, 7 $\alpha$  $\beta$ -H), and 5.6–5.9 ppm (multiplet, *J*<sub>6,7</sub> = 6 cps, *J*<sub>7,7a</sub> = 2.5 cps, 6-H and 7-H); mass spectrum 414 (M<sup>+</sup>, 4%), 371 (9%), and 354 (3%). *Anal.* Calcd for C<sub>25</sub>H<sub>34</sub>O<sub>5</sub>: C, 72.43; H, 8.27. Found: C, 72.30; H, 8.02.

**Hydrolysis and Oxidation of XIV to XVI.** XIV (114 mg) was dissolved in methanol (25 ml) and a solution of potassium bicarbonate (25 mg) in water (2.5 ml) was added. The reaction mixture was left at room temperature for 24 hr and then poured into water. The crude product (90 mg) was isolated by extraction with ethyl acetate, and was then oxidized using a 20% excess of Jones reagent in acetone (3 ml). After 5 min ethyl acetate and water were added. The organic layer was washed with water, and then dried and evaporated to give crude XVI (74 mg) which was purified by preparative tlc to give B-bishomo-5 $\alpha$ ,7 $\beta$  $\alpha$ -cycloandrosta-6-ene-3,6 $\alpha$ ,17-trione (XVI, 51 mg, 55%): mp 129–131°; [ $\alpha$ ]<sub>D</sub> +93°; ORD [ $\Phi$ ]<sub>600</sub> +310°, [ $\Phi$ ]<sub>389</sub> +358°, [ $\Phi$ ]<sub>356</sub> +2070°, [ $\Phi$ ]<sub>347</sub> +1810°, [ $\Phi$ ]<sub>341</sub> +1880°, [ $\Phi$ ]<sub>331</sub> +1560°, [ $\Phi$ ]<sub>317</sub> +2720°, [ $\Phi$ ]<sub>308</sub> +980°, [ $\Phi$ ]<sub>305</sub> +1430°, [ $\Phi$ ]<sub>300</sub>  $\pm$ 0°, [ $\Phi$ ]<sub>297</sub> -505°, [ $\Phi$ ]<sub>295</sub> -390°, [ $\Phi$ ]<sub>288</sub> -1420°, [ $\Phi$ ]<sub>285</sub> -1340°, [ $\Phi$ ]<sub>280</sub> -1470°, [ $\Phi$ ]<sub>249</sub> -390°, [ $\Phi$ ]<sub>233</sub> -1130°, [ $\Phi$ ]<sub>212</sub> -2060°;  $\nu_{\max}$  222 m $\mu$  ( $\epsilon$  8000);  $\nu_{\max}$  1730, 1710, 1690 cm<sup>-1</sup>; nmr 0.85 (18-H), 0.93 (19-H), 2.47 (4-H), 5.97 and 7.34 ppm (AB quartet, *J*<sub>6,7</sub> = 5.5 cps, 6-H and 7-H); mass spectrum 326 (M<sup>+</sup>, 22%), 311 (2%), and 308 (3%). *Anal.* Calcd for C<sub>21</sub>H<sub>28</sub>O<sub>6</sub>: C, 77.27; H, 8.03. Found: C, 77.21; H, 8.12.

**Hydrogenation of the Enone XVI to XVIII.** XVI (8 mg) in ethanol (1 ml) was added to prehydrogenated 10% palladium on carbon (5 mg) in ethanol (2 ml). The mixture was shaken in a hydrogen atmosphere for 30 min. The product XVIII was crystallized from ethyl acetate-hexane: mp 145–147°; nmr 0.90; (18-H), 1.07 (19-H), and 2.50 ppm (4-H); mass spectra 328 (M<sup>+</sup>, 100%), 313 (14%), 310 (7%), 300 (6%), 295 (7%), 284 (39%), 271 (12%), 269 (12%), 257 (25%), and 256 (26%).

**Deuteration of XVIII.** XVIII (3 mg) was dissolved in methanol-*d* (1 ml) containing a catalytic amount of sodium deuterioxide in deuterium oxide. The solution was refluxed for 20 hr. Most of the solvent was blown off with dry nitrogen, and the residue partitioned between ether and water. The ethereal solution was quickly washed, dried, and evaporated. The residue was redissolved in a few drops of ether and the solution was allowed to evaporate slowly in a sample tube in a dry atmosphere, producing crystals of nondeuterated XVIII, mp 140–144°. The mass spectrum indicated the following deuterated species: *d*<sub>7</sub> (13%), *d*<sub>8</sub> (34%), and *d*<sub>9</sub> (53%).

**Acknowledgment.** We wish to thank Dr. Laszlo Tökés for assistance in the interpretation of mass spectra.