clear filtrate, after concentration to 15 ml., was cooled to precipitate glutaric acid. Two recrystallizations from benzene gave 1.1 g. (69%) of glutaric acid (XI), m.p. 93–94°. Another crystallization did not change the melting point.

Anal. Calcd. for $C_5H_8O_4$: C, 45.45; H, 6.10; neut. equiv., 66.05. Found: C, 45.57, 45.62; H, 6.04, 6.07; neut. equiv., 66.0; radioactivity, 70.8, 71.4, 69.0, 70.2 (av. 70.4) μc./mole.

1,3-Dibenzamidopropane (XII) from Glutaric Acid (XI).[26]—A mixture of radioactive glutaric acid XII (0.50 g. or 0.0038 mole), sodium azide (1.04 g. or 0.0160 mole) and pure chloroform (25 ml.) was swept with a slow stream of nitrogen. The gases from the reaction mixture were passed up a vertical water-cooled condenser and then into aqueous barium hydroxide. Concentrated sulfuric acid (7 ml. or 0.1 mole) was added by drops to the stirred mixture at *ca.* 64° over a 15-min. period. Stirring and heating were continued for 2 hr.

Aqueous sodium hydroxide (60 ml. of a 15% solution) was added slowly with stirring and cooling. Benzoyl chloride (2.4 g. or 0.017 mole) was added and the mixture was shaken vigorously for 10 min. and intermittently for 5 hr. After an additional 15 hr. at room temperature, the two layers were separated and the organic layer was extracted thoroughly with chloroform. The combined chloroform solutions were dried with magnesium sulfate and boiled to remove all solvent. Two crystallizations of the residual oil from benzene gave 0.63 g. (59%) of 1,3-dibenzamidopropane (XII), m.p. 148.5–149° (cor.).

Anal. Calcd. for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43. Found: C, 72.6, 72.02; H, 6.39, 6.69; radioactivity, 0.8 ± 0.4 μc./mole.

Radioactivity Measurement.[27]—Samples to be analyzed were burned quantitatively to carbon dioxide and water, which were collected and measured manometrically. The carbon dioxide was bled into a Bernstein–Ballentine tube or an ionization chamber for counting. Individual radioactivity determinations have standard deviations of 2–3%.

Acknowledgment.—We are grateful to Research Corporation for a grant that supported much of this work and to R. Christian Anderson and David R. Christman for their help and advice. Some of the research was performed under the auspices of the U. S. Atomic Energy Commission.

(26) *Cf.* H. Wolff, "Organic Reactions," R. Adams, Ed., Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 307; S. Rothchild and M. Fields, *J. Org. Chem.*, **16**, 1080 (1951).

(27) R. C. Anderson, Y. Delabarre, and A. A. Bothner-By, *Anal. Chem.*, **24**, 1298 (1952).

A Steroidal Internal Displacement Reaction[1]

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Reaction of 3,5-cyclo-6β-methoxy-17β-tosyloxyandrostan-14α-ol with base yields 3,5-cyclo-6β-methoxy-14-androsten-17α-ol instead of fragmentation products. Base treatment of the *p*-toluenesulfonylhydrazone of 3β-acetoxy-14α-hydroxy-5-androsten-17-one affords the rearranged product 13α,14α-oxido-5-androsten-3β-ol.

The 5,10-, 8,9-, and 13,14-seco steroids contain medium sized rings incorporated into the steroid nucleus. It is desirable to synthesize these compounds in order to evaluate this structural variation on biological properties. An attractive route to a 13,14-seco compound involves fragmentation[2] of an appropriately substituted 1,3-diol monotosylate.

Starting with 5-androstene-3β,14α,17β-triol (I),[3] this was converted to the 3,17-ditosylate II. Selective methanolysis of the more reactive 3β-tosylate afforded the 3,5-cyclo derivative III. The necessary stereochemical arrangement of reactive centers is in principle present in III, *e.g.*, the *trans* antiparallel relationship of C-13–C-14 bond and the departing 17β-tosyloxy group to form a seco ketone by bond fragmentation.

Treatment of the 1,3-diol monotosylate III with potassium *t*-butoxide in boiling *t*-butyl alcohol led to the partial recovery of starting material with no detectable seco ketone as evidenced by the infrared spectrum. These conditions were found to be suitable for the fragmentation reaction in other 1,3-diol monotosylates.[2] Reaction of III under more vigorous conditions, with sodium hydride in tetrahydrofuran, which promoted irreversible alkoxide ion formation at C-14 led to a transformation product IV. The substance IV was characterized by the formation of a monoacetate on acetylation with acetic anhydride. The n.m.r. of IV showed the presence of one vinyl proton (4.84 τ).[4]

The transformation of IV to a substance of known structure was accomplished by acetolysis of the 3,5-cyclo steroid to the 3β-acetoxy-Δ^5 compound Va. Oxidation of Va with chromic acid led to the known 17-ketone VI.[3]

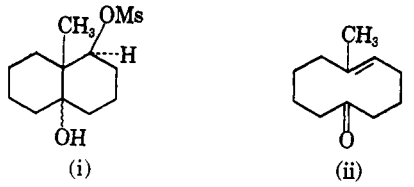
The substance V was also isolated from the reaction mixture and is related to IV by the presence of a 3β-hydroxy-Δ5 system generated from the 3,5-cyclo steroid. This change apparently occurred on the acidic alumina employed in the chromatographic separation.

Formation of the 17α-ol IV can be presumed to arise by intermediate formation of the highly strained 14α,17α-oxide compound VII formed by internal displacement, with attendant inversion at C-17, by the C-14 alkoxide ion. The strained intermediate VII undergoes further base-catalyzed elimination to IV.[5]

The absence of seco ketonic material arising from the four-center reaction is probably a result of the non-

(1) This investigation was supported by PHSR Grant AM-05183 from the National Institute of Arthritis and Metabolic Diseases.

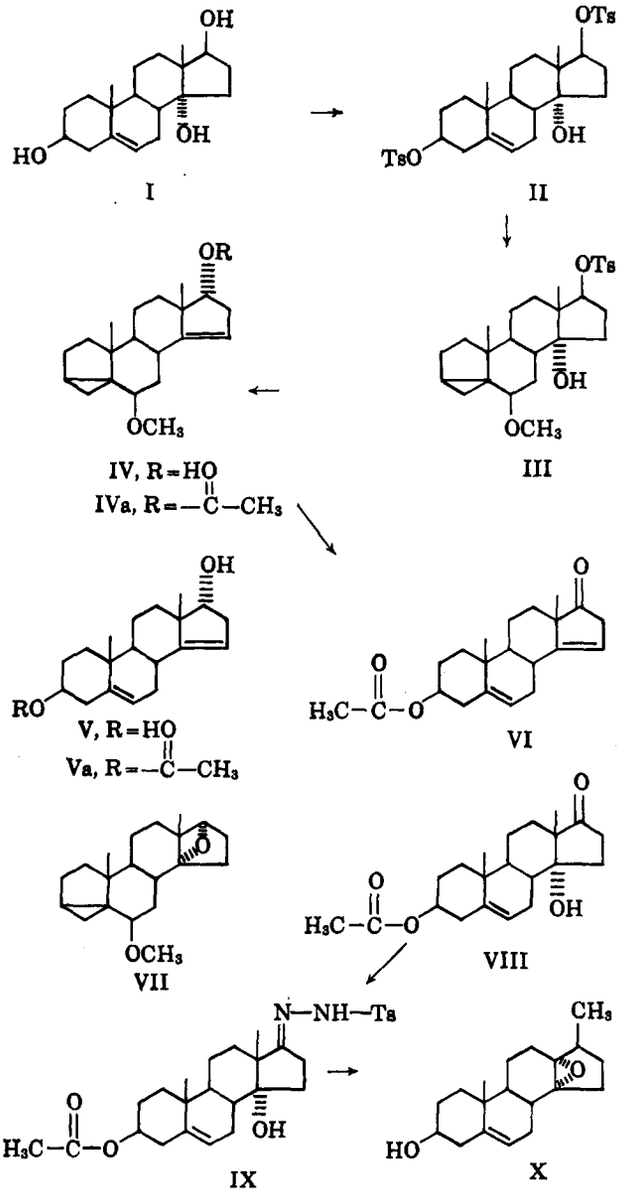
(2) R. B. Clayton, H. B. Henbest, and M. Smith, *J. Chem. Soc.*, 1982 (1957), report the fragmentation of the C-4–C-5 bond on base treatment of 3β-tosyloxy-5α-hydroxycholestane. P. S. Wharton, *J. Org. Chem.*, **26**, 4781 (1961), also has recently reported the facile fragmentation of the bicyclic 1,3-diol monomesylate (i) to (ii).



(i) (ii)

(3)(a) A. F. St. Andre, *et al.*, *J. Am. Chem. Soc.*, **74**, 5506 (1952). The stereochemistry of the hydroxyl at C-14 is alpha in I as demonstrated by (b) S. H. Eppstein, *et al.*, *ibid.*, **80**, 3382 (1958).

(4) The n.m.r. spectrum of 3β-acetoxy-5,14-androstadien-17β-ol showed the C-15 proton signal at 4.81 τ and the C-17α proton signal at 6.0 τ. In compound IV the C-17β proton signal is found at 6.04 τ. We thank Mr. W. V. Anderson for recording the n.m.r. spectra. The spectra were recorded at 60 Mc. on a Varian Associates HR4300 high resolution spectrometer on deuteriochloroform solutions of the steroids.



coplanarity of the reacting centers caused by conformational rigidity of ring D.[6]

It is well established that 1,3-diols undergo fragmentation reactions under acid-catalyzed conditions *via* carbonium ion intermediates.[7] A variant of this fragmentation method was investigated as a means of obtaining the desired 13,14-seco compound. Schechter and Friedman[8] have demonstrated that the base-catalyzed decomposition of *p*-toluenesulfonylhydrazones in protic solvents afford products characteristic of the intermediate formation of carbonium ions. In the present case, possible C-13–C-14 bond fission concerted

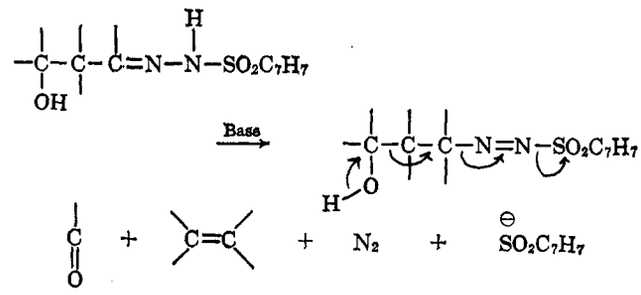


Figure 1

with a carbonium ion generated at C-17 *via* a *p*-toluenesulfonylhydrazone was attempted as a method of obtaining a seco compound. (See Fig. 1.)

Reaction of 3β-acetoxy-5-androsten-14α-ol-17-one[2] (VIII) with *p*-toluenesulfonylhydrazine afforded the hydrazone IX. Decomposition of IX with sodium in boiling ethylene glycol yielded a rearranged oxide X with little or no ketonic material present as judged by the infrared spectrum of the total reaction mixture.

The structure of X was established by the n.m.r. spectrum of X which showed the C-18 methyl signal as a doublet at 9.0 τ ($J \sim 7$ c.p.s.), and by the absence of hydroxyl absorption in the infrared spectrum. No proton signals characteristic of an ethylene oxide type were apparent in the n.m.r., indicating the tetrasubstituted nature of the oxide. The stereochemistry of X is assigned on its probable mode of formation which involves generation of a carbonium ion at C-17, followed by migration of the C-18 angular methyl group and collapse of the ion at C-13 by oxide formation.[9]

Experimental[10]

3β,17β-Ditosyloxy-5-androsten-14α-ol (II).—To a solution of 1.0 g. of the triol I in pyridine was added 3.3 g. of *p*-toluenesulfonyl chloride. The mixture was allowed to stand for 16 hr. at room temperature. The product was precipitated by pouring the reaction mixture into ice–water. Filtration and drying afforded 1.9 g. of crude II. An analytical sample was prepared by repeated crystallization from benzene, m.p. 126–127°, $[\alpha]^{24}D$ −38°; λ_{Nujol} 2.75 (OH), 6.23, 8.4, 8.5 μ (tosylate).

Anal. Calcd. for $C_{37}H_{42}O_7S_2$: S, 10.4. Found: S, 9.95.

3,5-Cyclo-6β-methoxy-17β-tosyloxy-androstan-14α-ol (III).—To a solution of 1.8 g. of the ditosylate II in 200 ml. of methanol and 25 ml. of acetone was added 4.0 g. of anhydrous potassium acetate. The mixture was refluxed for 3 hr. under a nitrogen atmosphere. The solvent was removed under reduced pressure, 200 ml. of water was added, and the mixture was extracted with chloroform. The chloroform extract was washed with water, dried over sodium sulfate, and the chloroform was removed under reduced pressure, to yield 1.5 g. of crude III. Crystallization from acetone–hexane gave analytical sample, m.p. 164–166°.

Anal. Calcd. for $C_{27}H_{38}O_5S$: C, 68.32; H, 8.07; S, 6.76. Found: C, 67.88; H, 7.82; S, 6.58.

(5) In footnote 2a discussion of the factors responsible for 1,3-oxide formation from 1,3-diol monosulfonates in fused ring systems is presented. The isomerization of 3α,5α-oxidocholestane to 3α-hydroxy-5-cholestene under mild acidic conditions is also reported.

(6) (a) F. V. Brutcher, Jr., and W. Bauer, Jr., *J. Am. Chem. Soc.*, **84**, 2236 (1962), discuss the three most probable conformations of Ring D in the steroids. Examination of Dreiding molecular models of compound III indicates that the dihedral angle between the departing tosylate group and the C-13–C-14 bond in both envelope and half chair conformations varies from 140–150°. In addition, the increased 1,3 interaction of a solvated 14α-hydroxy anion and the C-17α-hydrogen exerts its effect by further diminishing the dihedral angle and thereby favoring the internal displacement reaction to the 14α,17α-oxide. (b) E. J. Corey, R. B. Mitra, and H. Uda, *ibid.*, **85**, 362 (1963), have utilized fragmentation reactions of appropriately substituted 1,3-hydrindanediol monotosylates for introduction of cyclononene moiety in an elegant total synthesis of *d,l*-caryophyllene and its isomers.

(7) See H. Wasserman, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1955, p. 375. Direct acid treatment of a C-14α–C17β-diol would be expected to yield a 13,17-seco compound *via* the C-14 carbonium ion intermediate.

(8) H. Schechter and L. Friedman, *J. Am. Chem. Soc.*, **81**, 5512 (1959).

(9) Skeletal rearrangements have been previously observed in *p*-toluenesulfonylhydrazone decompositions. See (a) W. R. Bamford and T. S. Stevens, *J. Chem. Soc.*, 4735 (1952); (b) R. Hirschmann, C. S. Snoddy, Jr., C. F. Hiskey, and N. L. Wendler, *J. Am. Chem. Soc.*, **56**, 4013 (1954); (c) J. Elks, G. H. Phillipps, D. A. H. Taylor, and L. J. Wyman, *J. Chem. Soc.*, 1739 (1954); (d) W. F. Johns, *J. Org. Chem.*, **26**, 4583 (1961).

(10) Melting points were taken on a Fisher-Johns apparatus. A Perkin-Elmer Infracord was used to obtain infrared spectra. Rotations were determined in chloroform at 1% concentrations unless otherwise stated. Thin layer chromatographic data were obtained on Merck Silica Gel-G with a chloroform–ether solvent system. The microanalyses were performed by Berkeley Microanalytical Laboratory.

3,5-Cyclo-6β-methoxy-14-androsten-17α-ol (IV) and 5,14-Androstadiene-3β,17α-diol (V).—To a suspension of 0.5 g. of sodium hydride (50% in mineral oil) in 88 ml. of dry tetrahydrofuran under a nitrogen atmosphere was added dropwise a solution of 1.4 g. of III in 50 ml. of dry tetrahydrofuran. The reaction mixture was refluxed for 16 hr. under a nitrogen atmosphere, then cooled to room temperature, and the excess sodium hydride decomposed by dropwise addition of water. An additional 200 ml. of water was added and the mixture was extracted 3 times with 150-ml. portions of chloroform. The chloroform extract was washed with water, dried over sodium sulfate, and taken to dryness under reduced pressure. An infrared spectrum of the residue indicated the absence of carbonyl absorption. The residue was dissolved in benzene and chromatographed on Merck acid washed alumina. Elution with benzene afforded 471 mg. of IV. An analytical sample was prepared by crystallization from hexane, m.p. 128–130°; $[\alpha]^{24}D$ +52; λ_{Nujol} 3.1 μ (–OH); n.m.r.: 8.84 (15-proton), 6.04 doublet (17-proton, J = 5 c.p.s.), 6.65 (methoxy), 8.93 (19-methyl), 8.98 τ (18-methyl).

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.61; H, 9.79.

Elution with chloroform afforded 70 mg. of V. An analytical sample was prepared by crystallization from acetone–ether, m.p. 193–195°, $[\alpha]^{24}D$ −81°; λ_{Nujol} 3.0 μ (–OH); n.m.r.: 4.62 (6-proton), 4.88 (15-proton), 6.04 doublet (17-proton, J = 6 c.p.s.), 8.96 (19-methyl), and 9.0 τ (18-methyl).

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.52. Found: C, 79.12; H, 9.79.

3,5-Cyclo-6β-methoxy-14-androsten-17α-ol 17-Acetate (IVa).—To a solution of 0.1 g. of IV in 5 ml. of pyridine was added 5 ml. of acetic anhydride. The solution was allowed to stand for 16 hr. and the solvents were removed under reduced pressure. Attempts to crystallize the oil that remained were unsuccessful. An analytical sample was prepared by sublimation at 100° (0.005 mm.), $[\alpha]^{25}D$ +58; λ_{Nujol} 5.75 and 8.0 μ (CH_3COO—).

Anal. Calcd. for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 76.10; H, 8.61.

3β-Acetoxy-5,14-androstadien-17α-ol (Va).—To a solution of 10 mg. of IV in 1.0 ml. of glacial acetic acid was added 1.0 mg. of *p*-toluenesulfonic acid and the reaction mixture was allowed to stand for 4 hr. The mixture was diluted with water and extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and the ether removed under reduced pressure, affording 10 mg. of a clear oil, λ_{Nujol}, 2.9 (OH), 5.75 and 8.0 μ (CH_3COO—). Thin layer chromatography of this material revealed that it was homogeneous.

3β-Acetoxy-5,14-androstadien-17-one (VI).—To a solution of 10 mg. of the oil Va in 1 ml. of acetone an acidic solution of chromium trioxide[11] was added dropwise until a slight excess was present. The solution was then filtered through Celite, diluted with water, and extracted with chloroform. The chloroform extract was washed with water, dried over sodium sulfate, and the solvent was removed under reduced pressure, affording 10 mg. of a clear oil. Thin layer chromatography revealed that the oil was homogeneous and had thin layer chromatographic mobility in two solvent systems identical to that of an authentic sample of 3β-acetoxy-5,14-androstadien-17-one[3]; λ_{Nujol} 5.75, 8.0 (CH_3COO—), and 5.8 μ (17-ketone).

***p*-Toluenesulfonylhydrazone of 3β-Acetoxy-14α-hydroxy-5-androsten-17-one (IX).**—To a solution of 0.5 g. of 3β-14α-hydroxy-5-androsten-17-one[3] (VIII) in 25 ml. of ethanol was added 0.28 g. of *p*-toluenesulfonylhydrazine and 0.05 g. of *p*-toluenesulfonic acid. The reaction mixture was refluxed for 2 hr. and cooled to room temperature. Under reduced pressure half of the solvent was removed and addition of 50 ml. of ice–water precipitated the product. Filtration and drying afforded 0.389 g. of crude product. An analytical sample was prepared by repeated crystallization from methanol, m.p. 251–252°; λ_{Nujol} 2.8 (14-OH), 3.1, 6.28, 7.1, 7.5, and 8.6 (tosylhydrazone), and 5.75 and 8.0 μ (acetate).

Anal. Calcd. for $C_{27}H_{38}O_5N_2S$: N, 5.5. Found: N, 5.1.

13α,14α-Oxido-5-androsten-3β-ol (X).—To a solution of 0.5 g. of sodium in 75 ml. of dry ethylene glycol under a nitrogen atmosphere was added 0.5 g. of the tosylhydrazone IX. The solution was refluxed for 1 hr. under a nitrogen atmosphere, cooled to room temperature, diluted with 200 ml. of ice–water and extracted with chloroform–ether. The extract was washed with water, dried over sodium sulfate, and the solvent was removed under reduced pressure affording 0.35 g. of residue. An frared spectrum of the residue revealed the absence of carbonyl and tosylhydrazone absorption. Thin layer chromatography showed principally one component. The residue was dissolved in benzene and chromatographed on Merck acid-washed alumina. Elution with ether afforded 127 mg. of X. An analytical sample was prepared by crystallization from dioxane–water, m.p. 139–142°, $[\alpha]^{25}D$ −101°; λ_{Nujol} 2.8 μ (–OH); n.m.r.: 4.57 (6-proton), 9.02 and 9.13 doublet (17-methyl, J = 7 c.p.s.), and 9.02 τ (19-methyl).

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found, C, 78.86; H, 9.71.

(11) (a) K. Bowden, *et al.*, *J. Chem. Soc.*, 39 (1946); (b) C. Djerassi, *et al.*, *J. Org. Chem.*, **21**, 1548 (1956).

Organoboron Compounds. XVII.[1] Chemistry of a Compound with Neighboring Borono, Ethynyl, and Amine Functional Groups[2]

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The synthesis of 2-(*o*-boronophenylethynyl)pyridine (I) and conversion to 2-[β-hydroxy-β-(*o*-boronophenyl)-vinyl]pyridine (II) are reported. Synergetic activity of the borono and amine groups in these molecules was investigated by means of a reaction with chloroethanol.

8-Quinolineboronic acid[4,5] and 2-(2-boronophenyl)-benzimidazole[1] displace chloride from chloroethanol considerably faster than do equimolar mixtures containing benzeneboronic acid and quinoline or 2-phenylbenzimidazole. The enhanced activity of the former compounds was attributed to cooperative action of the borono and amine functions made possible by the proximity of these groups in a given molecule. As a further test of the role of molecular geometry on the chemical properties of the borono and amine groups, we undertook a study of 2-(*o*-boronophenylethynyl)-pyridine (I). In this molecule the groups are sufficiently separated that direct interaction would not be expected[6]; therefore the reaction pathways available to 8-quinolineboronic acid and the boronophenylbenzimidazole should not be available to compound I.

(1) Paper XVI: R. L. Letsinger and D. B. MacLean, *J. Am. Chem. Soc.*, **85**, 2230 (1963).

(2) This research was supported in part by the National Science Foundation.

(3) Dow Chemical Co. Fellow, Lubrizol Corp. Fellow.

(4) R. L. Letsinger and S. Dandegaonker, *J. Am. Chem. Soc.*, **81**, 498 (1958).

(5) R. L. Letsinger, S. Dandegaonker, W. J. Vullo, and J. D. Morrison, *ibid.*, **85**, 2223 (1963).

(6) On the basis of normal bond lengths and angles it is estimated that the minimum distance separating boron and nitrogen in I would be 4.8 Å., while the minimum distance between hydrogen (of BOH) and nitrogen would be 2.9 Å.