evaporated to give 3.47 g of an oil that was purified by partition chromatography[10] on diatomaceous silica using a heptane–methanol (1:1) solvent system. The fraction with peak hold-back volume 4.0 (v_m/v_s = 2.7) was evaporated; recrystallization of the residue from acetone–hexane gave 238 mg (7%) of **2,3-dihydro-5-hydroxy-3,3-dimethyl-2-(4-morpholinyl)-6-phenylbenzofuran** (**3a**) as white crystals, mp 215–217°.

Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.80; H, 6.97; N, 4.29.

The fraction with peak hold-back volume 6.0 was evaporated; the residue was recrystallized from acetone–hexane to furnish 2.033 g (70%) of **2,3-dihydro-5-hydroxy-3,3-dimethyl-2-(4-morpholinyl)-7-phenylbenzofuran** (**4a**) as white crystals, mp 164–165°.

Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.53; H, 7.10; N, 4.26.

Reaction of 4.70 g (37.5 mmol) of 1-piperidyl-1-propene (**2b**) and 4.60 g (25 mmol) of 2-phenyl-1,4-benzoquinone (**1a**) in benzene gave 3.65 g of **2,3-dihydro-5-hydroxy-3-methyl-7-phenyl-2-(1-piperidyl)benzofuran** (**4b**) as crystals, mp 130–133°, by direct crystallization. Partition chromatography of the material in the filtrate using a heptane–methanol (1:1) system afforded an additional 1.13 g (62%) of crystals, mp 135–137°, in that fraction with peak hold-back volume 3.4 (V_m/V_s = 2.5). A sample was recrystallized from ether–hexane to give white crystals, mp 135–137°.

Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.91; H, 7.51; N, 4.52.

Treatment of 1.38 g (10 mmol) of 2-methoxy-1,4-benzoquinone (**1b**) with 1.49 g (10 mmol) of isobutenylmorpholine (**2a**) in methylene chloride, solvent removal, and trituration of the residue with ether gave 2.44 g (87%) of **2,3-dihydro-5-hydroxy-6-methoxy-3,3-dimethyl-2-(4-morpholinyl)benzofuran** (**3b**) as crystals, mp 157–161°. A sample recrystallized from methanol had mp 168–169°.

Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.49; H, 7.58; N, 5.01. Found: C, 64.23; H, 7.29; N, 4.71.

Oxidation of the 2-Amino-2,3-dihydrobenzofurans.—The following experiment illustrates the general procedure. A solution of 1.080 g (2.0 mmol) of ferric chloride hexahydrate in 7.5 ml of water was added dropwise with stirring to a suspension of 650 mg (1.0 mmol) of 2,3-dihydro-5-hydroxy-3,3-dimethyl-2-(4-morpholinyl)-7-phenylbenzofuran (**4a**) in 75% methanol. The mixture was stirred for 3 hr after completion of the addition, at which time it was bright yellow. The solid was collected by filtration and dissolved in methylene chloride. This solution was passed through a magnesia–silica gel column using methylene chloride as the eluting solvent. The yellow eluate was evaporated to give a residue that was recrystallized twice from ether to give 340 mg (67%) of **α-(6-phenyl-2-*p*-quinoyl)isobutyraldehyde** (**6**) as orange crystals: mp 141–142°; λ_{max} 291 mμ (ε 4840), 314 (5340).

Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.30; H, 5.63; N, 0.0.

In the manner described above, treatment of 120 mg (0.36 mmol) of 2,3-dihydo-5-hydroxy-3,3-dimethyl-2-(4-morpholinyl)-6-phenylbenzofuran (**3a**) with 270 mg (1.0 mmol) of ferric chloride hexahydrate furnished 43 mg (43%) of **α-(5-phenyl-2-*p*-quinoyl)isobutyraldehyde** (**5**) as needles, mp 127–128°, after recrystallization from ether–hexane: λ_{max} 300 mμ (ε 5970), 312 (6480).

Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.65; H, 5.42; N, 0.0.

Registry No.—**3a**, 16793-13-8; **3b**, 16793-14-9; **4a**, 16793-15-0; **4b**, 16793-16-1; **5**, 14348-69-7; **6**, 16793-18-3.

Acknowledgment.—The author is indebted to Mr. C. Pidacks and his staff for the partition chromatography, to Mr. W. Fulmor and his associates for the spectral data, and to Mr. L. Brancone and his group for the microanalyses.

(10) For a complete description of this technique, as developed by Mr. C. Pidacks of these laboratories, see M. J. Weiss, R. E. Schaub, G. R. Allen, Jr., J. F. Poletto, C. Pidacks, R. B. Conrow, and C. J. Coscia, *Tetrahedron*, **20**, 357 (1964).

Preparation of A-Ring Conjugated Enones and the Corresponding α,β-Epoxy Ketones of 17β-Acetoxy-5α-androstane

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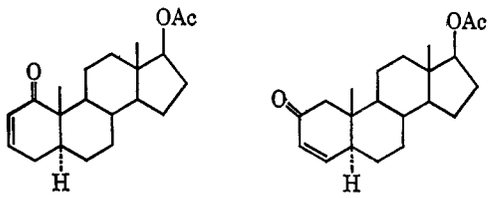
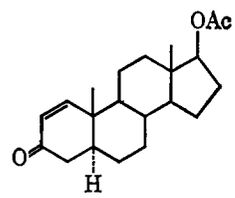
In connection with other studies, the title compounds were needed. While the A-ring conjugated enones (**1–4**) are already known, there were some different observations between those reported by earlier authors[1] and ours during the course of preparing the enones (**1**, **2**, and **4**). The epoxy ketones (*e.g.* **5**, **14**, **24**, and **26**) are believed to be interesting compounds for CD[2a] and biological[2b] studies. These compounds, except for **5**, have not been reported to date.

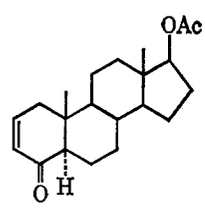


1

2

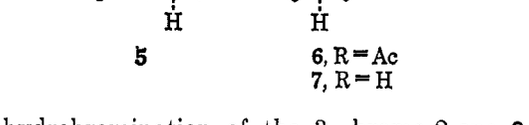


3



4

Reductive elimination of the 1α,2α-epoxy-3-one **5**[3] with 60% $NH_2NH_2 \cdot H_2O$ gave the enol **6** in 57% yield, which upon oxidation afforded the 2-en-1-one **1**. In our hands, the reaction of the epoxy ketone **5** with 100% $NH_2NH_2 \cdot H_2O$ according to Djerassi, *et al.*,[1a] who obtained only the enol **6** (40%), yielded a mixture of the enol **6** (12%) and the 2-ene-1α,17β-diol **7** (37%). Furthermore, the use of 95% $NH_2NH_2 \cdot H_2O$[1b] could not prevent cleavage of the C_{17} acetoxyl group.



5 **6**, R = Ac; **7**, R = H

Dehydrobromination of the 3α-bromo-2-one **9**, derived from the bromohydrin **8**,[4] with Li_2CO_3 alone af-

(1) (a) C. Djerassi, D. H. Williams, and B. Berkoz, *J. Org. Chem.*, **27**, 2205 (1962); (b) P. D. Klimstra and R. E. Counsell, *J. Med. Chem.*, **8**, 48 (1965); (c) P. D. Klimstra, U. S. Patent 3,166,578 (1965); *Chem. Abstr.*, **62**, 9207a (1965).

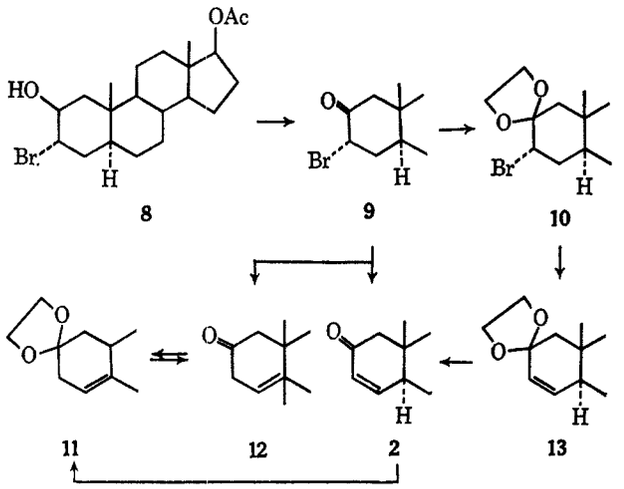
(2) (a) K. Kuriyama, H. Tada, Y. K. Sawa, S. Itô, and I. Itoh, *Tetrahedron Lett.*, 2539 (1968); (b) Dr. Miyake of our laboratory, unpublished results.

(3) W. M. Hoehn, *J. Org. Chem.*, **23**, 929 (1958).

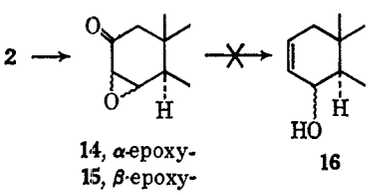
(4) Kindly supplied by Dr. Komeno of our laboratory.

forded a mixture of the 3-en-2-one **2** and the isomeric 4-en-2-one **12**, whose separation either by column chromatography or by preparative tlc was unsuccessful, but recrystallization from a large amount of ether gave the pure enone **2** (mp 134–136°; $[\alpha]D$ +105.0°). Although the physical values are considerably different from those reported (mp 87–90°; $[\alpha]D$ +8°),[1b] the structure of our compound **2** is undoubtedly correct judging from its typical spectral properties and from the chemical transformations shown in Scheme I.

SCHEME I



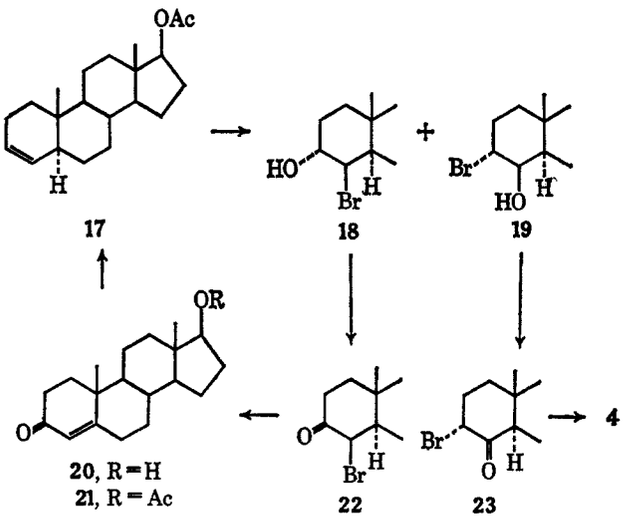
Ketalization of the dehydrobromination product (a mixture of **2** and **12**) gave only the Δ^4-2-ketal **11**, which on hydrolysis afforded the 4-en-2-one **12** (mp 146–148°; $[\alpha]D$ +128.3°). Dehydrobromination of the bromo ketal **10** with *t*-BuOK in DMSO and subsequent acetylation led to the Δ^3-2-ketal **13**, which on a brief treatment with diluted hydrochloric acid gave the enone **2**.



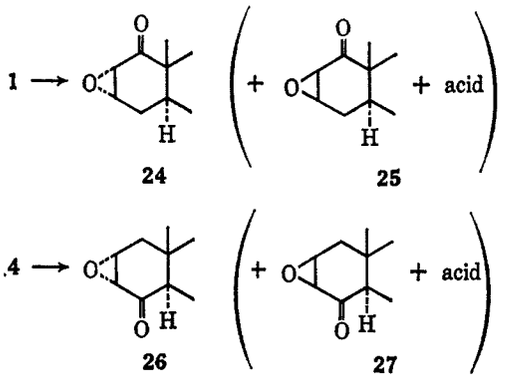
14, α-epoxy-
15, β-epoxy-

Epoxidation of the enone **2** with alkaline hydrogen peroxide according to Hoehn[3] afforded the 3α,4α-epoxy-2-one **14** (mp 184–185°; $[\alpha]D$ +58.9°) together with the 3β,4β-epoxy-2-one **15** (mp 163–165°; $[\alpha]D$ +114.9°). Configuration of the epoxy ring was confirmed by the chemical shift of the 19-methyl group in the nmr spectrum. Reductive elimination of the epoxy ketone **14**, however, gave only an intractable material.

An alternative route to the 2-en-4-one **4** *via* the olefin **17**, prepared by hydroboration of testosterone **20** followed by treatment with Ac_2O,[5] was then examined. Reaction of the olefin **17** with hypobromous acid either in dioxane[6] or in DMSO gave a mixture of bromohydrins, which was chromatographed to give the 3α-bromo-4β-ol **19** (mp 212–213°; $[\alpha]D$ −7.1°) and the 4β-bromo-3α-ol **18** (mp 195–196°; $[\alpha]D$ +2.8°). Both isomeric bromohydrins were characterized as the corresponding bromo ketones **23**[7] (mp 152–154°; $[\alpha]D$ −131.4°) and **22** (mp 171–172°; $[\alpha]D$ −98.8°). Treatment of both bromo ketones **22** and **23** with Li_2CO_3 afforded respective enones **21** and **4**. The former enone **21** was proved to be testosterone acetate.



Epoxidation of the 2-en-1-one **1** with alkaline hydrogen peroxide according to Julian, *et al.*,[8] afforded the 2α,3α-epoxy-1-one **24** (mp 174–175°; $[\alpha]D$ +20.6°) as a major product. The epimeric 2β,3β-epoxy-1-one **25** was only detected in the nmr spectrum of the residue after separation of the α isomer. Unexpectedly, an acidic component was isolated as a minor product, whose structure is now under study.



An analogous result was obtained for epoxidation of the 2-en-4-one **4**. The 2α,3α-epoxy-4-one **26** (mp 122–124°; $[\alpha]D$ +9.0°) was a major product and the epimeric 2β,3β-epoxy-4-one **27** was only detected in the nmr spectrum of the residue after separation of the α isomer. In this case, an acidic component after esterification showed many spots on tlc.

Experimental Section[9]

17β-Acetoxy-5α-androst-2-en-1α-ol (6).—Reductive cleavage of the epoxy ketone **5**[3] with 60% $NH_2NH_2 \cdot H_2O$ alone, in place of

(5) *Cf.* L. Caglioti, G. Cainelli, G. Maina, and A. Selva, *Gazz. Chim. Ital.*, **92**, 309 (1962); *Tetrahedron*, **20**, 957 (1964).

(6) Klimstra and Counsell reported isolation of only one bromohydrin, **19** (mp 166–168°; $[\alpha]D$ −4.5°), without description of the yield.[1c]

(7) In the literature,[1b,c] mp 130–132° (hemihydrate) and $[\alpha]D$ −79.5° are reported.

(8) P. L. Julian, W. Cole, E. W. Meyer, and B. M. Regan, *J. Amer. Chem. Soc.*, **77**, 4601 (1955).

(9) Melting points were observed in capillaries and are corrected. Specific rotations were measured in $CHCl_3$ (*c* 1) with Perkin-Elmer polarimeter, Type 141. The infrared spectra were recorded in $CHCl_3$ with JASCO DS-201 B spectrometer. The nmr spectra were obtained on a Varian A-60A spectrometer using $CDCl_3$ solutions. The chemical shifts are expressed in parts per million downfield from a standard (TMS). The ORD and CD curves were measured in MeOH on a JASCO Model ORD/UV-5 equipped with CD attachment. Data are presented as follows: ORD λ_{max} ([Φ]); CD λ_{max} ([θ]).

100% $NH_2NH_2 \cdot H_2O$ in *i*-PrOH containing AcOH,[1a] yielded the enol **6** (57%; mp 144–153°). After recrystallization it melted at 154–156°, $[\alpha]D$ +122.1°.

17β-Acetoxy-5α-androst-2-en-1-one (1).—Oxidation of the enol **6** with Jones reagent[10] gave the enone **1**: mp 193–194° (from *i*-PrOH); $[\alpha]D$ +124.5°; nmr, δ 6.67 (C_3-H, doublet of triplets, J = 10.0 and 3.5 cps), 5.79 (C_2-H, doublet of triplets, J = 10.0 and 1.5 cps), 1.06 (19-Me), and 0.18 ppm (18-Me); ORD 360 (−1810) and 305 mμ (+8290); CD 335 mμ (−5990).

Dehydrobromination of 17β-Acetoxy-3α-bromo-5α-androstan-2-one (9).—A solution of the bromo ketone **9** (2.0 g) in DMF (20 ml) was refluxed with Li_2CO_3 (1.2 g) for 4 hr under nitrogen. Dilution with water and extraction with benzene afforded a halogen-free solid, which was triturated with ether to give a crystalline product (1.3 g; tlc, two spots). Recrystallization from a large amount of ether gave **17β-acetoxy-5α-androst-3-en-2-one (2)**: mp 134–136°; $[\alpha]D$ +105.0°; ir, 1725 and 1670 cm^{-1}; nmr δ 6.55 (C_4-H, doublet of doublets, J = 10.0 and 2.0 cps), 5.97 (C_3-H, octet, J = 10.0, 3.0, and 1.0 cps), 0.89 (19-Me, d, J = 1.0 cps), 0.81 ppm (18-Me); uv max (95% EtOH), 233 mμ (ε 8500) and 312 (56); CD 347 (−760) and 294 mμ (+470).

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.21; H, 9.11.

17β-Acetoxy-2,2-ethylenedioxy-5α-androst-4-ene (11).—A mixture of the above mentioned dehydrobromination product (2.0 g), ethylene glycol (4 ml), and benzene (100 ml) containing *p*-TsOH·H_2O (120 mg) was refluxed for 3 hr using a water separator. The usual treatment and crystallization of a crude product from EtOH gave 1.48 g (65%) of the Δ^4-2-ketal **11**: mp 159–160°; $[\alpha]D$ +0.5°; nmr, δ 5.25 (C_4-H, m), 1.15 (19-Me), and 0.82 ppm (18-Me).

Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.84; H, 9.00.

17β-Acetoxy-5α-androst-4-en-2-one (12).—The Δ^4-2-ketal **11** (1.0 g) was heated with 80% aqueous AcOH (20 ml) on a boiling-water bath for 8 min and poured into water. A precipitate was filtered (0.9 g; mp 141–144°) and recrystallized from EtOH to give 415 mg of the enone **12**: mp 146–148°; $[\alpha]D$ +128.3°; ir, 1720 cm^{-1}; nmr, δ 5.29 (C_4-H, m), 1.01 (19-Me), and 0.82 ppm (18-Me); ORD 307 (+6790) and 271 mμ (−5040); CD 290 mμ (+8900).

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.16; H, 9.12.

17β-Acetoxy-3α-bromo-2,2-ethylenedioxy-5α-androstane (10).—A mixture of the bromo ketone **9** (2.0 g), ethylene glycol (3 ml), *p*-TsOH·H_2O (970 mg), and benzene (100 ml) was refluxed for 6 hr using a water separator. The usual treatment and subsequent acetylation gave a solid, which on recrystallization from acetone yielded 1.8 g of the bromo ketal **10**: mp 197–199°; $[\alpha]D$ +64.6°; nmr, δ 4.18 ppm ($C_{3\beta}$-H, m, $W_{1/2}$ = 5 cps).

Anal. Calcd for $C_{23}H_{35}BrO_4$: C, 60.65; H, 7.75; Br, 17.55. Found: C, 61.06; H, 7.84; Br, 17.73.

17β-Acetoxy-2,2-ethylenedioxy-5α-androst-3-ene (13).—A solution of the bromo ketal **10** (1.5 g) and *t*-BuOK (2.2 g) in DMSO (60 ml) was left at room temperature for 24 hr. Dilution with water and extraction with benzene gave a solid (1.16 g; tlc, one spot), which on acetylation yielded the amorphous Δ^3-2-ketal **13** (1.16 g; tlc, one spot): nmr, δ 5.53 (C_3-H and C_4-H, s, two protons), 0.90 (19-Me), and 0.78 ppm (18-Me).

Hydrolysis of the Δ^3-2-Ketal 13.—Treatment of the Δ^3-2-ketal **13** (563 mg) in acetone (5 ml) with 1 *N* HCl (0.5 ml) at room temperature for 20 min gave the enone **2** (485 mg; tlc, one spot). After recrystallization from ether, it melted at 134–135°: $[\alpha]D$ +104.1°.

Epoxidation of the Enone 2.—To a solution of the enone **2** (4.6 g) in MeOH (120 ml) was added 30% H_2O_2 (5 ml) and 10% NaOH (1 ml) in MeOH (25 ml) at 0°. After 30 min at room temperature, a crystalline solid was filtered (2.2 g, mp 171–175°). The filtrate was concentrated *in vacuo* and a precipitate was separated (0.9 g, mp 155–163°). Dilution of the second filtrate and extraction with ether gave a solid, which on trituration with ether yielded the third crop (252 mg). The first two crops were chromatographed on silica gel (300 g). Elution with EtOAc–benzene (3:97) and recrystallization from EtOH gave **17β-acetoxy-3α,4α-epoxy-5α-androstan-2-one (14)**: mp 184–185°; $[\alpha]D$ + 58.9°; nmr, δ 3.20 and 3.08 (C_3-H and C_4-H, AB quartet, J = 3.5 cps), 0.83 (19-Me), and 0.78 ppm (18-Me); ORD 322 (+2450) and 282 mμ (−1350); CD 303 mμ (+3120).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.97; H, 8.84.

The third crop was purified by preparative tlc and crystallized from EtOH to yield **17β-acetoxy-3β,4β-epoxy-5α-androstan-2-one (15)**: mp 163–165°; $[\alpha]D$ +114.9°; nmr, δ 3.30 and 3.20 (C_3-H and C_4-H, AB quartet, J = 4.0 cps), 1.09 (19-Me), and 0.78 ppm (18-Me); ORD 329 (+6580) and 286 mμ (−4850); CD 308 mμ (+9490).

Anal. Calcd for $C_{21}H_{30}O_4$: C, C, 72.80; H, 8.73. Found: C, 72.81; H, 8.77.

17β-Acetoxy-5α-androst-3-ene (17).—A solution of **testosterone (20**, 5.0 g) in diglyme (150 ml) was treated with a large excess of diborane for 1 hr at room temperature. Acetic anhydride (80 ml) was added and the mixture was refluxed for 1.5 hr (all operations were carried out under nitrogen). The reaction mixture was concentrated *in vacuo*, poured into water, and extracted with benzene. The product (6.2 g) was chromatographed on Al_2O_3 (250 g), and elution with benzene gave a solid (2.9 g; mp 93–102°; tlc, one spot), which was recrystallized twice to afford 1.35 g (25%) of the olefin **17**: mp 117–118°; $[\alpha]D$ +28.2° (lit.[11] mp 117–118°; $[\alpha]D$ +42.0°); nmr, δ 5.56 (C_3-H, d, J = 10 cps), 5.25 (C_4-H, d, J = 10 cps), and 0.79 ppm (19- and 18-Me).

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.59; H, 10.28.

Reaction of the Olefin 17 with Hypobromous Acid.—To a solution of the olefin **17** (632 mg) in dry DMSO (18 ml) was added water (0.1 ml) and N-bromosuccinimide (NBS) (712 mg) with cooling under nitrogen. After stirring for 40 min at room temperature, the reaction mixture was diluted with water (120 ml) and extracted with ether to give a product (812 mg; tlc, two spots), which was chromatographed on silica gel (40 g). Elution with EtOAc–benzene (2:98) gave a bromohydrin (263 mg; 32%; mp 205–208°), which on recrystallization from acetone afforded **17β-acetoxy-3α-bromo-5α-androstan-4β-ol (19)**: mp 212–213° dec; $[\alpha]D$ −7.1°; nmr, δ 4.35 ($C_{3\beta}$-H, q, J = 2.3 cps), 3.87 ($C_{4\alpha}$-H, m, $W_{1/2}$ = 5.5 cps), 1.03 (19-Me), and 0.78 ppm (18-Me).

Anal. Calcd for $C_{21}H_{33}BrO_3$: C, 61.01; H, 8.04; Br, 19.32. Found: C, 61.11; H, 8.09; Br, 19.56.

Further elution with EtOAc–benzene (5:95) gave another bromohydrin (426 mg; 52%; mp 192–194°), which on recrystallization from acetone afforded **17β-acetoxy-4β-bromo-5α-androstan-3α-ol (18)**: mp 195–196° dec; $[\alpha]D$ +2.8°; nmr, δ 4.24 ($C_{3\beta}$-H, m), 4.06 ($C_{4\alpha}$-H, m), 1.08 (19-Me), and 0.78 ppm (18-Me).

Anal. Calcd for $C_{21}H_{33}BrO_3$: C, 61.01; H, 8.04; Br, 19.32. Found: C, 61.28; H, 8.10; Br, 19.53.

17β-Acetoxy-3α-bromo-5α-androst-4-one (23).—The bromohydrin **19** (1.0 g) in acetone (40 ml) was oxidized with chromic acid to give 987 mg of the bromo ketone **23**: mp 154–156°; $[\alpha]D$ −131.4°; nmr, δ 4.28 ($C_{3\beta}$-H, t, J = 3 cps), 3.10 ($C_{5\alpha}$-H, doublet of doublets, J = 10.8 and 4.2 cps), 0.78 (18-Me), and 0.75 ppm (19-Me); ORD 334 (−1460) and 288 mμ (+1830); CD 309 mμ (−27700).

Anal. Calcd for $C_{21}H_{31}BrO_3$: C, 61.31; H, 7.60; Br, 19.42. Found: C, 61.15; H, 7.58; Br, 19.39.

17β-Acetoxy-4β-bromo-5α-androstan-3-one (22).—Oxidation of the bromohydrin **18** (1.0 g) in acetone (40 ml) with Jones reagent yielded 968 mg of the bromo ketone **22**: mp 174–175°; $[\alpha]D$ −98.8°; nmr, δ 4.13 ($C_{4\alpha}$-H, m, $W_{1/2}$ = 6.5 cps), 3.10 ($C_{2\beta}$-H, triplet of doublets, J = 15.0 and 6.0 cps), 1.28 (19-Me), and 0.80 ppm (18-Me); ORD 334 (−7480) and 285 mμ (+7600); CD 309 mμ (−14100).

Anal. Calcd for $C_{21}H_{31}BrO_3$: C, 61.31; H, 7.60; Br, 19.42. Found: C, 61.52; H, 7.71; Br, 19.79.

17β-Acetoxy-5α-androst-2-en-4-one (4).—A solution of the bromo ketone **23** (1.56 g) in DMF (18 ml) was refluxed with Li_2CO_3 (940 mg) for 1.5 hr under nitrogen. Dilution with water and extraction with ether gave a product (1.29 g; mp 181–185°), which on recrystallization from EtOH yielded 1.05 g (84%) of the enone **4**: mp 187–188°; $[\alpha]D$ +9.0° (lit.[1b] mp 182–184°; $[\alpha]D$ +7.5°); ir, 1726 and 1676 cm^{-1}; nmr, δ 6.80 (C_2-H, octet, J = 10.0, 5.0, and 3.0 cps), 6.03 (C_2-H, octet, J = 10.0,

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2.3, and 1.0 cps), 0.87 (19-Me), and 0.80 ppm (18-Me); ORD 352 (−3250) and 297 mμ (+6700); CD 331 mμ (−7760).

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.06; H, 9.15.

Testosterone Acetate (21). A.—Acetylation of **testosterone 20** in the usual way gave **21**: mp 141–142°; $[\alpha]_D$ +96.2°.

B.—The bromo ketone **22** (300 mg) was dehydrobrominated with Li_2CO_3 (180 mg) in DMF (4 ml) to give the enone **21** (221 mg; mp 136–138°, mmp 138–140°; $[\alpha]_D$ +93.1°), whose tlc showed a faint spot of the enone **3**, besides a main spot of **21**.

Epoxidation of the Enone 1.—To a solution of the enone **1** (600 mg) in MeOH (20 ml) and CH_2Cl_2 (6 ml) was added 30% H_2O_2 (1.8 ml) and 4 *N* NaOH (0.9 ml) at 0°, and the reaction mixture was kept in an ice chest at 3° for 48 hr. Dilution with water and extraction with CH_2Cl_2 gave a product (423 mg; mp 167–174°), which on recrystallization from EtOH afforded 297 mg (47%) of **17β-acetoxy-2α,3α-epoxy-5α-androstan-1-one (24)**: mp 177–178°; $[\alpha]_D$ +20.6°; nmr, δ 3.43 ($C_{3\beta}$-H, m), 3.13 ($C_{2\beta}$-H, d, J = 3.5 cps), 1.01 (19-Me), and 0.78 ppm (18-Me); ORD 342 (−2110) and 298 mμ (+3670); CD 321 mμ (−4080).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.41; H, 8.74.

The residue after separation of the α isomer **24** showed, in addition to the signals which are due to the α isomer, a doublet at 3.21 ppm (J = 5 cps) and a singlet at 1.22 ppm, ascribable to the presence of the β isomer **25**. The aqueous solution, after extraction of the neutral component, was acidified with dilute HCl, extracted with CH_2Cl_2, esterified with CH_2N_2, and separated by preparative tlc to afford an ester (145 mg, 20%).

Epoxidation of the Enone 4.—A solution of the enone **4** (507 mg) in CH_2Cl_2 (5 ml) and MeOH (10 ml) was treated with 30% H_2O_2 (1.5 ml) and 4 *N* NaOH (0.75 ml) at 0°. Working up as mentioned above gave 494 mg of a neutral product, which on recrystallization from ether afforded 319 mg (60%) of **17β-acetoxy-2α,3α-epoxy-5α-androstan-4-one (26)**: mp 123–125°; $[\alpha]_D$ +9.0°; nmr, δ 3.50 ($C_{2\beta}$-H, m), 3.23 ($C_{3\beta}$-H, d, J = 3.8 cps), 0.76 (19-Me), and 0.79 ppm (18-Me); ORD 324 (−1850), 314 (−1620), and 280 mμ (+3060); CD 307 (−2850) and 300 mμ (−3020).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 73.02; H, 8.71.

The 2β,3β-epoxy-4-one **27** was detected by the additional signals (multiplet at 3.05 and singlet at 1.10 ppm) in the nmr spectrum of the residue after separation of the α isomer. An acidic component (30 mg) was isolated but resisted purification, even as a methyl ester as shown by a multiplicity of spots on tlc.

Registry No.—**1**, 6199-40-2; **2**, 68-61-1; **4**, 65-01-0; **6**, 5846-70-8; **10**, 16801-95-9; **11**, 16801-96-0; **12**, 16801-97-1; **13**, 16801-98-2; **14**, 16801-85-7; **15**, 16801-86-8; **17**, 1236-50-6; **18**, 16801-88-0; **19**, 2311-73-1; **21**, 1045-69-8; **22**, 16801-91-5; **23**, 1242-08-6; **24**, 16801-93-7; **26**, 16801-94-8.

The Alkaloids of *Tabernaemontana crassa*. Crassanine, a New Oxindole Alkaloid

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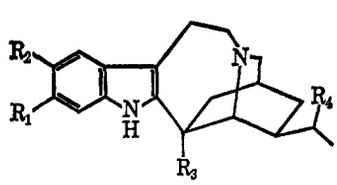
As part of an extended chemotaxonomic study of the genus *Tabernaemontana* (Apocynaceae),[1] we now describe the results of a study of the alkaloids of the African species, *Tabernaemontana crassa* Benth.

The major alkaloid of *T. crassa* proved to be the known ibogamine-type base, conopharyngine (**1**);[2] an amorphous base, which we were unable to completely purify by chromatography, was the second most abundant alkaloid. This latter base, which was assigned the structure of 20-hydroxyconopharyngine (**2**), was purified instead by a new procedure which should be widely applicable for the isolation of related bases.[3] Thus, the reaction of impure **2** with benzyl chloroformate in pyridine afforded the crystalline carbobenzoxy ester **3**, from which pure **2** was readily regenerated by hydrogenolysis in the presence of palladium.

The assigned structure of **2** fully agreed with its spectral properties. Its ultraviolet absorption spectrum was that of a typical 5,6-dimethoxyindole; indeed, it was essentially identical with that of conopharyngine (**1**). In addition, the nmr spectrum of **2** was similar to that of its unmethoxylated analog, heyneanine (**4**),[4] except that the spectrum of **2** clearly showed the presence of the 5,6-dimethoxyindole system in the form of methoxyls at δ 3.78 and 3.86 and a pair of unsplit aromatic protons at 6.71 and 6.83. Furthermore, the mass spectrum of **2** was exactly analogous to the published spectrum of heyneanine (**4**),[4] except that the fragments from **2** containing the indole nucleus were 60 mass units heavier than those from **4** because of two methoxy substituents on the aromatic ring.



1, $R_1 = R_2 = OCH_3$; $R_3 = COOCH_3$; $R_4 = H$
2, $R_1 = R_2 = OCH_3$; $R_3 = COOCH_3$; $R_4 = OH$
3, $R_1 = R_2 = OCH_3$; $R_3 = COOCH_3$; $R_4 = OCO_2CH_2C_6H_5$
4, $R_1 = R_2 = H$; $R_3 = COOCH_3$; $R_4 = OH$
5, $R_1 = R_2 = OCH_3$; $R_3 = R_4 = H$
6, $R_1 = R_2 = OCH_3$; $R_3 = H$; $R_4 = OH$

The structure of **2** was confirmed by its chemical conversion into ibogaline (**5**), using the general degradative scheme which has been employed previously with other 20-hydroxyibogamine-type bases.[5–8] Thus, hydrolysis of the ester function of **2**, followed by decarboxylation, yielded the amorphous 20-hydroxyibogaline (**6**). Reaction of **6** with tosyl chloride in pyridine gave the corresponding quaternary tosylate (**7**) which was reduced directly by lithium aluminum hydride to give ibogaline (**5**). After this work was completed, a preliminary report appeared on the isolation of 20-hydroxyconopharyngine (**2**) from *Conopharyngia jol-*

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