afforded a pure sample, mp 145–146° (lit.[21] mp 145°). Analysis of the crude reaction mixture by vpc revealed only two major products (*ca.* 1:7 ratio) which were identified as acetophenone (10%) and diphenacyl; traces of phenacyl chloride and *t*-butylphenylacetate were also detected. Traces of benzoic acid were isolated from the aqueous extracts.

The previous reaction was repeated at one-twelfth the scale. The reaction was quenched with 6 ml of glacial acetic acid in *ca.* 1 sec. Conventional work-up afforded a 0.46-g mixture of diphenacyl–phenacyl chloride–acetophenone (*ca.* 1:7:7, vpc). A 39 and 32% yield of acetophenone and phenacyl chloride, respectively, were obtained by nmr integration.

Reaction of Phenacyl Chloride with Potassium *t*-Butoxide at Benzene Reflux.—The procedure was identical with that of the previous large-scale, room temperature experiment up to the termination of the addition of the phenacyl chloride–benzene solution. At this point, the benzene mixture was refluxed for 1.5 hr with stirring. The reaction mixture was worked up as usual leaving an oily residue.

Vpc showed three major components in a 6:3:1 ratio. These were collected by vpc and identified as *t*-butyl phenylacetate (V), dibenzyl ketone (VI), and ω-benzylacetophenone (VII), respectively, by comparison of their physical and spectral properties with independently synthesized samples. Phenacyl chloride and acetophenone were minor components (<5%) in the residue. Acidification of the aqueous extracts afforded 0.84 g (21%) of phenylacetic acid, mp 74–76° (lit.[22] mp 77°).

(21) C. Weygand and W. Meusel, *Chem. Ber.*, **76**, 498 (1943).
(22) B. Sobin and G. B. Bachman, *J. Amer. Chem. Soc.*, **57**, 2458 (1935).

The reaction was conducted several times on a smaller scale. From the vpc and nmr spectrum of these crude reaction mixtures, the yield of V (30%), VI (15%), and VII (5%) was calculated. The V:VI:VII product ratio was identical after either 0.5- or 1.5-hr reflux.

Changing the solvent to cyclohexene gave the same products with slightly different ratios; the absence of 7-benzoylnorcarane was confirmed by vpc of the reaction mixture and synthetic norcaryl ketone.

Control Experiments.—In separate experiments, dibenzyl ketone, ω-benzylacetophenone, 7-benzoylnorcarane, and diphenacyl were reacted with a fourfold excess of potassium *t*-butoxide at benzene reflux for 1.5 hr. After work-up, all were recovered in quantitative or near quantitative yield.

Reaction of *t*-Butylphenylacetate with Potassium *t*-Butoxide.—Potassium *t*-butoxide (0.535 g, 5.00 mmol) was added to 8 ml of anhydrous benzene. To this stirred slurry, *t*-butylphenylacetate (0.30 g, 1.6 mmol) was added and the mixture was refluxed for 1.5 hr and worked up in the usual manner.

Unreacted starting material (0.218 g, 73%) was obtained from the organic phase. From the combined aqueous extracts, a white, crystalline acid, mp 74–76°, was isolated (0.08 g, 21%), whose nmr and ir spectra were identical with the spectra of phenylacetic acid.

Registry No.—Phenacyl chloride, 532-27-4; 3-bromo-2,4-diphenylfuran, 23346-66-9; II, 23346-65-8.

Acknowledgment—R. J. D. P. thanks Colgate Palmolive Co. and the Wright Fund for financial assistance.

Methylenation of Unsaturated Ketones. VIII.[1] Reaction of $\Delta^{1,4}$-, $\Delta^{1,4,6}$-, and $\Delta^{4,6}$-3-Keto Steroids with Phenyl(trichloromethyl)mercury[2]

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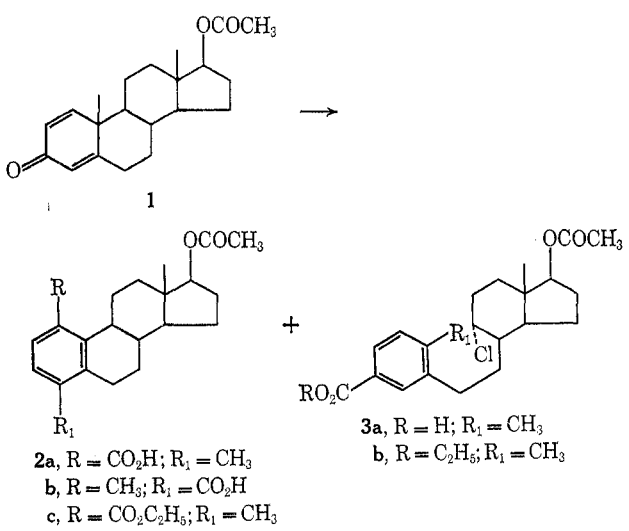
The $\Delta^{1,4}$- and $\Delta^{1,4,6}$-3-keto steroids **1** and **4** undergo dienol–benzene-type rearrangements on exposure to phenyl(trichloromethyl)mercury in benzene to yield ring-A aromatic carboxylic acids (**2a** and **3a** from **1**) and **5** from **4**. Although the $\Delta^{4,6}$-3 ketone **8a** is apparently resistant to attack by the mercurial reagent in boiling benzene, the corresponding 3β-acetoxy and 3-cycloethylenedioxy derivatives **8b** and **8c** are converted into the 6α,7α-dichloromethylene adducts **10a** and **10b** (plus **10d**), respectively, under the same conditions.

Phenyl(trichloromethyl)mercury is an exceptionally effective reagent for the dichloromethylenation of carbon–carbon double bonds. In an extensive series of investigations, Seyferth and coworkers showed that various olefins, as well as aliphatic α,β-unsaturated ketones, esters, and nitriles, react with the organomercurial in boiling benzene to afford the corresponding dichlorocyclopropanes in good yield.[3] This paper describes the results of an investigation aimed at evaluating phenyl(trichloromethyl)mercury as a reagent for preparing dichloromethylene steroids from linear and cross-conjugated dienone and trienone precursors.

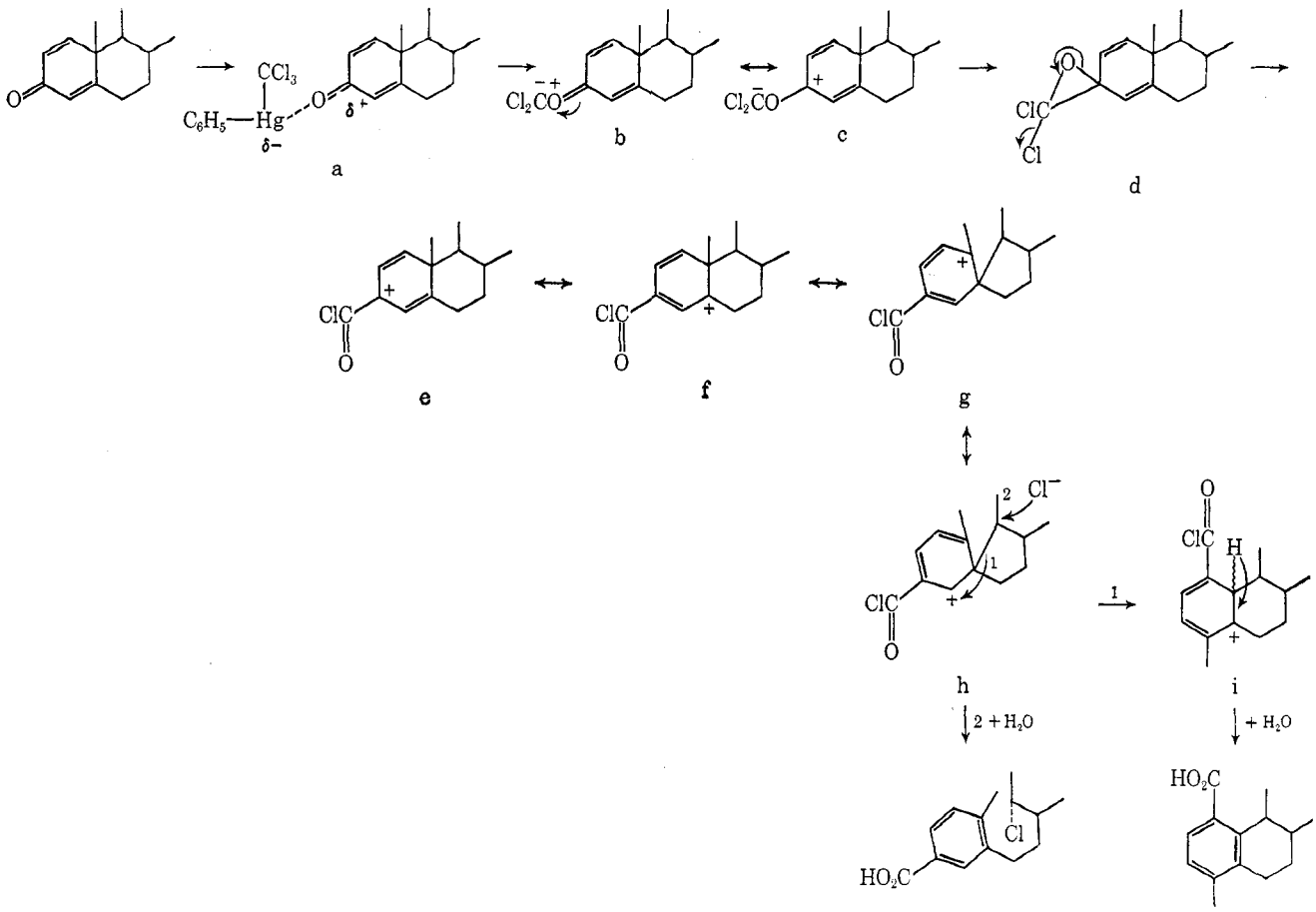
Treatment of 17β-acetoxyandrosta-1,4-dien-3-one (**1**)[4] with 20 equiv of phenyl(trichloromethyl)mercury in boiling benzene followed by chromatography of the crude reaction mixture afforded the ring-A aromatic



acids **2a** (12%) and **3a** (13%).[5] The structure of the seco acid **3** follows from its elemental analysis and

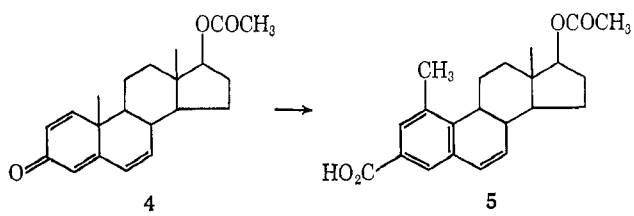
(1) Part VII: C. Beard, B. Berkoz, N. H. Dyson, I. T. Harrison, P. Hodge, L. H. Kirkham, G. S. Lewis, D. Giannini, B. Lewis, J. A. Edwards, and J. H. Fried, *Tetrahedron*, **25**, 1219 (1969).
(2) Publication 363 from the Syntex Institute of Organic Chemistry.
(3) D. Seyferth, J. M. Burlitch, R. J. Minasz, J. Y.-P. Mui, H. D. Simmons, Jr., A. J. H. Trieber, and S. R. Dowd, *J. Amer. Chem. Soc.*, **87**, 4259 (1965).
(4) R. B. Woodward, H. H. Inhoffen, H. O. Larson, and K. Menzel, *Chem. Ber.*, **86**, 594 (1953).
(5) Some difficulty was experienced with the removal of phenylmercuric chloride from the reaction mixture. In this experiment the isolated yield proved to be a poor measure of reaction efficiency, since substantial product losses were incurred during chromatographic purification.

SCHEME I



infrared, mass, and proton magnetic resonance spectroscopy. The latter determination shows an aromatic methyl proton resonance at 2.38 ppm in addition to three aromatic protons consisting of a singlet at 2.38 ppm (H-4) and an AB pattern centered at 7.56 ppm (J = 8.0 Hz, H-1 and H-2). The C-9 chloro substituent of **3a** is assigned the axial (α) stereochemistry, since the H-9 signal (broad singlet, $W_{1/2}$ = 0.07 ppm at 100 MHz) of the ethyl ester **3b** exhibits the splitting pattern typical of an equatorial proton coupled to several vicinal protons.[6] The tetracyclic carboxylic acid bears methyl and carboxyl substituents at the C-1 and C-4 positions of the A ring, as judged by the presence of signals for an aromatic methyl group (singlet at 2.22 ppm) and two aromatic (*ortho*) protons (AB pattern centered at 6.95 ppm, J = 8.0 Hz). The 1-carboxy-4-methyl structure **2a** is tentatively assigned to this product by analogy to the established course of the dienol–benzene rearrangement.[7a] However, the 1-methyl-4-carboxy substitution pattern **2b** cannot be ruled out on the basis of the available evidence.

17β-Acetoxyandrosta-1,4,6-trien-3-one (**4**)[8] was readily aromatized by heating with 1.1 equiv of the mercurial reagent in boiling benzene to give 1-methyl-3-carboxy-



estra-1,3,5(10),6-tetraene (**5**) in 56% yield. The pmr spectrum of this substance exhibits a singlet at 2.60 ppm (aromatic methyl), an AB pattern centered at 6.23 ppm ($J_{6,7}$ = 10.0 Hz, H-6 and H-7), and two doublets at 7.60 and 7.70 ppm ($J_{2,4}$ = 2.0 Hz, H-2 and H-4) in agreement with the 1,3-disubstituted estratetraene system present in **5**.

The ease with which phenyl(trichloromethyl)mercury induces the $\Delta^{1,4}$-3-ketone system to undergo a dienol–benzene-type rearrangement prompted a study of the reaction of **1** with sodium trichloroacetate, an alternate source of dichlorocarbene.[9] In this case treatment of **1** with 29 equiv of the sodium salt in boiling diglyme afforded a complex mixture of products from which a low yield (3.8%) of the seco acid **3a** was obtained after repeated chromatography. A similar result has been reported for the reaction of **1** with difluorocarbene (generated from sodium difluorochloroacetate in boiling diglyme), the only aromatic product of this reaction being 4-methylestra-1,3,5(10)-trien-17β-ol acetate (obtained in 2.5% yield).[1]

The foregoing results suggest that the aromatization reactions of **1** and **4** are assisted by participation of

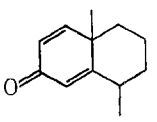
(6) For examples illustrating the use of band width at half-height in determining the axial or equatorial orientation of an alicyclic methine proton, see A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 1350 (1964), and references cited therein.

(7) For comprehensive reviews, see (a) N. L. Wendler in "Molecular Rearrangements," Part 2, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, Chapter 16; (b) B. Miller in "Mechanism of Molecular Migrations," Vol. 1, B. S. Thyagarajan, Ed., Interscience Publishers, Inc., New York, N. Y., 1968, pp 275–285.

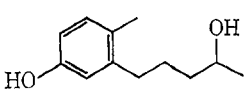
(8) G. Rosenkranz, C. Djerassi, S. Kaufmann, J. Pataki, and J. Romo, *Nature*, **165**, 814 (1950).

(9) W. M. Wagner, *Proc. Chem. Soc.*, 229 (1956).

mercury, with the rearrangement possibly being initiated by association of the carbonyl group with the mercurial reagent rather than a free carbene[10] (see a, Scheme I). Loss of phenylmercuric chloride leads, *via* the resonance-stabilized zwitterions b and c, to the intermediate oxide d. Lewis acid promoted opening of the oxide d followed by loss of chloride ion generates the chloroformyl mesomeric cation species e–i, which give rise to the aromatic acids **2a** and **3a** after hydrolysis of the intermediate acid chloride. Evidence for the existence of the acid chloride as the initial product follows from the isolation of the ethyl ester **2c** when the crude product obtained from reaction of **1** with the mercurial is allowed to stand in chloroform solution containing ethanol. Support for the intermediacy of the dichloro epoxide d is also provided by the recent observations of Seyferth and Tronich, which show that perchlorothiiranes are formed by reaction of thiophosgene and thiobenzophenone with phenyl(dichlorobromomethyl)mercury.[11] As in the case of dienol–benzene and dienone–phenol rearrangements,[7] the presence of a 6,7 double bond alters the course of the mercurial-promoted rearrangement of the $\Delta^{1,4,6}$-3 ketone **4**, the product **5** being formed by a methyl migration to the C-1 position. The isolation of the seco acid **3a** is of interest, since this is the first product of C_9–C_{10} bond cleavage to be identified from dienone–phenol- or dienol–benzene-type rearrangements in the steroid series.[7] However, Kropp has shown that the bicyclic dienone **6** rearranges in part to the monocyclic phenol **7** by acid catalysis.[12]

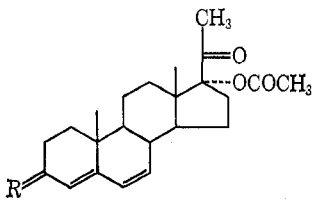


6

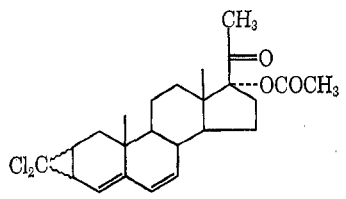


7

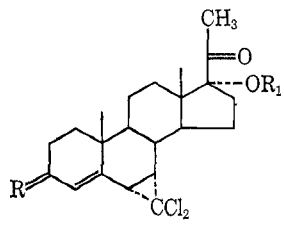
The reaction of the $\Delta^{4,6}$-pregnadienes **8a**,[13] **8b**,[14] and **8c**[15] with phenyl(trichloromethyl)mercury was next investigated, since these substances are not susceptible to the aromatization process. The $\Delta^{4,6}$-3 ketone **8a** appeared to be resistant to attack by the mercurial in boiling benzene. Under essentially the same conditions the allylic acetate **8b** yielded two products identified as 17α-acetoxy-2ξ,3ξ-dichloromethylenepregna-4,6-dien-20-one (**9**, 26%) and the noncrystalline 3β,17α-diacetoxy-6α,7α-dichloromethylenepregn-4-en-20-one (**10a**, 30%). The latter substance was characterized as 17α-acetoxy-6α,7α-dichloromethylenepregn-4-ene-3,20-dione (**10b**) by selective hydrolysis of the 3-acetate of **10a** followed by oxidation of the resulting allylic alcohol with manganese dioxide. The formation of 17α-acetoxypregna-2,4,6-trien-20-one (**11**), the precursor of the 2ξ,3ξ-dichloromethylene adduct **9**, is attributed to the action of the electrophilic mercurial reagent or dichlorocarbene on the allylic acetoxy group rather than phenylmercuric chloride, since **8b** was recovered unchanged after prolonged treatment with the latter substance in boiling benzene.

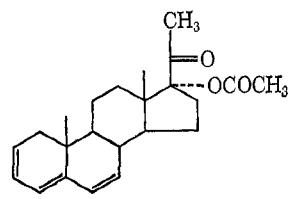


8a, R = O
b, R = β-OCOCH$_3$; α-H
c, R = cycloethylenedioxy



9

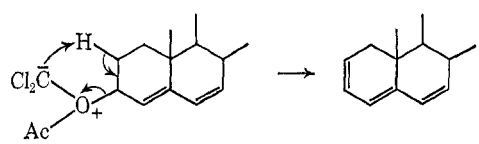




11

10a, R = β-OCOCH$_3$, α-H; R_1 = COCH$_3$
b, R = O; R_1 = COCH$_3$
c, R = O; R_1 = H
d, R = cycloethylenedioxy; R_1 = COCH$_3$

A possible mechanism to account for the formation of the intermediate **11** is as follows.



The assignment of the 6α,7α stereochemistry to the dichloromethylene group of adducts **10a–10d** is supported by the rotatory dispersion curve of **10b**, which is in good agreement with the curves reported for various 6α,7α-methylene- and 6α,7α-difluoromethylene-Δ^4-3 ketones.[1]

The ketal derivative **8c** is the most suitable starting material for the synthesis of the 6α,7α-dichloromethylene-Δ^4-3 ketone **10b**. Thus reaction of **8c** with an excess of the mercurial for 8 days in boiling benzene afforded directly the Δ^4-3-keto adduct **10b** in 40% yield *via* mercury salt catalyzed cleavage of the intermediate Δ^4-3-ketal adduct **10d**.[16] The latter substance was also obtained in 15% yield from this reaction.

(10) W. E. Parham and J. R. Potoski have suggested that the cleavage of certain allylamines by phenyl(trichloromethyl)mercury is initiated by attack of the mercurial reagent on the nitrogen atom instead of dichlorocarbene. See *J. Org. Chem.*, **32**, 278 (1967). See also D. Seyferth, M. E. Gordon, and R. Damrauer, *ibid.*, **32**, 496 (1967).

(11) D. Seyferth and W. Tronich, *J. Amer. Chem. Soc.*, **91**, 2138 (1969).

(12) P. J. Kropp, *ibid.*, **85**, 3280 (1963).

(13) R. Sciaky, *Gazz. Chim. Ital.*, **91**, 545 (1961).

(14) D. J. Marshall, P. F. Morand, C. Revesz, and R. Gaudry, *J. Med. Chem.*, **7**, 355 (1964).

(15) M. J. Weiss, J. F. Poletto, G. R. Allen, Jr., R. F. Schaub, and I. Ringler, *ibid.*, **7**, 804 (1964).

(16) The use of metal salts (*e.g.*, magnesium sulfate) for the cleavage of Δ^4-3 ketals to the corresponding Δ^4-3 ketones has been reported: J. J. Brown, R. H. Lenhard, and S. Bernstein, *Experientia*, **18**, 309 (1962).

Experimental Section[17]

Preparation of Phenyl(trichloromethyl)mercury.—The procedure of Seyferth and Burlitch[18] was modified as follows. A solution of phenylmercuric bromide (15.0 g) in dry tetrahydrofuran (300 ml) and chloroform (30.0 g) was cooled to −80° in acetone–Dry Ice and treated portionwise with stirring with 15.0 g of freshly prepared potassium *t*-butoxide (containing 1 molar equiv of *t*-butanol) during 20 min. The reaction mixture was stirred at −80° for 2 hr and then allowed to warm to room temperature. Water (500 ml) was added and the product was isolated by extraction with methylene dichloride. The crystalline residue (19.2 g), containing unreacted phenylmercuric bromide, was dissolved in benzene and percolated through a column of neutral alumina (200 g) to give 15.0 g of phenyl(trichloromethyl)mercury, mp 117–119° (lit.[18] mp 116.5–118°).

Reaction of 17β-Acetoxyandrosta-1,4-dien-3-one (1) with Phenyl(trichloromethyl)mercury.—A solution of **1** (2.0 g) and phenyl(trichloromethyl)mercury (2.8 g) in benzene was heated under reflux with stirring for 84 hr with further additions of 1.40 g and 0.70 g of mercurial reagent being made at 24- and 48-hr intervals. The precipitated phenylmercuric chloride was removed by filtration of the cooled reaction mixture and the resulting solution was evaporated to dryness. The residue was dissolved in ethyl acetate and chromatographed on 150 g of silica gel. Elution with ethyl acetate–acetic acid (200:1) provided a series of crystalline fractions from which the following compounds were obtained by preparative tlc[19] with benzene–acetic acid (49:1).

Compound **2a** (264 mg) gave the following data: mp 208–210° (from acetone–hexane); $[\alpha]_D$ +247°; λ_{max} 242 mμ (log ε 3.78); ν_{max} 3400, 1730, 1700, 1680, 1585, and 1245 cm^{-1}; nmr 0.83 (s, H-18), 1.98 (s, H-17β-acetoxy), 2.22 (s, CH_3-4), and 6.85 and 7.05 ppm (AB pattern, $J_{2,3}$ = 8.0 Hz, H-3 and H-2, respectively).

Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 73.76; H, 8.11.

Compound **3a** (310 mg) gave the following data: mp 133–136° (from hexane); $[\alpha]_D$ −9°; λ_{max} 238 mμ (log ε 4.14) and 270 (sh, 2.99); ν_{max} 3430, 1740, 1690, 1620, 1580, and 1250 cm^{-1}; nmr 0.83 (H-18), 2.03 (s, H-17β-acetoxy), 2.38 (s, aromatic CH_3), 4.3–4.9 (m, H-9β and H-17α), 7.25, 7.89 (AB pattern, $J_{2,3}$ = 8.0 Hz, H-3 and H-2, respectively), and 7.92 ppm (s, H-4); mass spectrum *m/e* 292 (M^+ for ^{35}Cl) and 294 (M^+ for ^{37}Cl).

Anal. Calcd for $C_{22}H_{29}O_4Cl$: C, 67.25; H, 7.44; Cl, 9.02. Found: C, 67.43; H, 7.41; Cl, 8.86.

The ethyl ester **3b** was prepared as follows. A solution of **3a** (130 mg) in dry benzene (5 ml) and thionyl chloride (1 ml) was heated under reflux for 2 hr and the solvents were evaporated to dryness. The residue was dissolved in 8 ml of benzene–pyridine (3:1) containing ethanol (2 ml) and after 2 hr the solvents were evaporated and the resulting oil was purified by preparative tlc with ethyl acetate–hexane (1:9). The pmr spectrum (100 MHz) of the resulting noncrystalline ethyl ester **3b** shows resonances at 0.84 (s, H-18), 1.38 (t, J = 7 Hz, CH_3CH_2O), 2.04 (s, H-17β-acetoxy), 2.37 (s, aromatic CH_3), 4.31 and 4.43 (AB pattern, J = 7.0 Hz, CH_3CH_2O), 4.57 (broad s, $W_{1/2}$ = 0.07 ppm, H-9β), 4.73 (ill-resolved m, H-17α), 7.19 and 7.78 (AB pattern, J = 8.0 Hz, H-1 and H-2, respectively), and 7.83 ppm (s, H-4). When the crude reaction mixture, obtained by treating **1** (2.0 g) with phenyl(trichloromethyl)mercury as described above, was allowed to stand for 7 days in chloroform (500 ml) containing ethanol, purification by preparative tlc yielded **2a** (84 mg), **3a** (350 mg), and the tetracyclic ethyl ester **2c** (190 mg): mp 116–118°; $[\alpha]_D$ +226°; λ_{max} 243 mμ (log ε 3.87) and 285 (3.13); ν_{max} 1740, 1715, 1590, 1280, and 1250 cm^{-1}; nmr 0.83 (s, H-18), 1.18 (t, J = 7 Hz, CH_3CH_2O), 2.02 (s, H-17β-acetoxy), 2.23 (s, CH_3-4), 4.22 and 4.42 (AB pattern, J = 7.0 Hz, CH_3-CH_2O), 4.5–5.0 (m, H-17α), and 7.01 and 7.42 ppm (AB pattern, $J_{2,3}$ = 8.0 Hz, H-3 and H-2, respectively).

Anal. Calcd for $C_{24}H_{32}O_4$: C, 74.96; H, 8.39; O, 16.64. Found: C, 74.92; H, 8.34; O, 16.75.

Reaction of 17β-Acetoxyandrosta-1,4,6-trien-3-one (4) with Phenyl(trichloromethyl)mercury.—A solution of **4** (5.0 g) and phenyl(trichloromethyl)mercury (6.6 g) in benzene (700 ml) was heated under reflux for 26 hr. The precipitated phenylmercuric chloride was removed by filtration and the solvent was evaporated to yield an oil which was dissolved in ethyl acetate and adsorbed on a column of silica gel (400 g). Elution with ethyl acetate provided 2.6 g of a mixture of starting **4** and phenylmercuric chloride. Further purification by preparative tlc with ethyl acetate–benzene (1:49) yielded pure **4** (740 mg). Continued elution of the column with ethyl acetate–acetic acid (49:1) gave 17β-acetoxy-1-methylestra-1,3,5(10),6-tetraene-3-carboxylic acid (**5**, 2.4 g): mp 272–275° (from acetone); $[\alpha]_D$ −143°; λ_{max} 235 mμ (log ε 4.62), 260 (sh, 3.81) and 310 (3.12); ν_{max} 1740, 1685, and 1245 cm^{-1}; nmr (100 mHz) 0.85 (s, H-18), 2.05 (s, H-17β-acetoxy), 2.60 (s, CH_3-1), 5.90, 6.49 (pair of d with additional splitting, $J_{6,7}$ = 10.0 Hz, H-6 and H-7), and 7.60 and 7.70 ppm (pair of d, $J_{2,4}$ = 2.0 Hz, H-2 and H-4).

Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.12; H, 7.35. Found: C, 73.81; H, 7.25.

Reaction of 17β-Acetoxyandrosta-1,4-dien-3-one (1) with Sodium Trichloroacetate.—A solution of **1** (660 mg) and sodium trichloroacetate (11.0 g) dissolved in 75 ml of dry diglyme was added dropwise during 1.5 hr to 50 ml of diglyme maintained at 130–140°. The reaction mixture was kept at 140° for 15 min after completion of the addition, then cooled, filtered, and evaporated to dryness under reduced pressure. The resulting brown oil was dissolved in methylene chloride and adsorbed on a column of 100 g of silica gel. Elution with methylene chloride–ethyl acetate (1:1) gave impure **1**. Continued elution with ethyl acetate–acetic acid (49:1) gave 150 mg of acidic mixture, which was purified by preparative tlc with ethyl acetate–acetic acid (49:1) to give the secoacid **3a** (30 mg), mp 130–131°, identical by mixture melting point and infrared spectral comparison with seco acid obtained by reaction of **1** with phenyl(trichloromethyl)-mercury.

Reaction of 3β,17α-Diacetoxypregna-4,6-dien-20-one (8b) with Phenyl(trichloromethyl)mercury.—A solution of **8b** (960 mg) and phenyl(trichloromethyl)mercury (1.14 g) in benzene (240 ml) was heated under reflux for 5 days. Removal of the solvent followed by purification of the resulting product by preparative tlc with ethyl acetate–hexane (3:7) afforded the following compounds.

The 2ξ,3-ξ-dichloromethylene adduct (**9**, 330 mg) gave the following data: mp 215° dec (from methanol); λ_{max} 251 mμ (log ε 4.32); ν_{max} 1720, 1710, and 1260 cm^{-1}; nmr 0.68 (s, H-18), 0.97 (s, H-19), 2.02 (s, H-17α-acetoxy), 2.06 (s, H-21), 5.45 (broad s, H-4), and 5.63 and 5.96 ppm (AB pattern, J = 11.0 Hz, H-6 and H-7).

Anal. Calcd for $C_{24}H_{30}O_3Cl_2$: C, 65.90; H, 6.91; Cl, 16.21. Found: C, 65.96; H, 7.28; Cl, 16.39.

The 6α,7α-dichloromethylene adduct **10a** (358 mg) was obtained as an oil.

17α-Acetoxy-6α,7α-dichloromethylenepregn-4-ene-3,20-dione (10b).—Adduct **10a** (358 mg) was dissolved in methanol–water (5:1, 30 ml) containing sodium hydroxide (0.2 g) and the resulting solution was kept at room temperature for 4 hr. Acetic acid (0.2 ml) and water (200 ml) were added and the product was isolated by extraction with diethyl ether. The resulting oil (300 mg) was oxidized by stirring with manganese dioxide (3.6 g) in chloroform (20 ml) for 2 hr to yield a mixture of two products separable by preparative tlc with ethyl acetate–hexane (3:7) into the following compounds.

The 17-acetate **10b** (100 mg) gave the following data: mp 188° (from acetone–hexane); $[\alpha]_D$ +81°; RD $[\Phi]_{600}$ +270°, $[\Phi]_{386}$ +3380°, $[\Phi]_{376}$ +3110°, $[\Phi]_{369}$ +3560°, $[\Phi]_{350}$ +3160°, $[\Phi]_{353}$ +2525°, $[\Phi]_{345}$ +1625°, $[\Phi]_{336}$ +2615°, $[\Phi]_{307}$ +8340°, $[\Phi]_{298}$ +6630°, $[\Phi]_{289}$ +3970°, $[\Phi]_{283}$ +3605°, $[\Phi]_{267}$ +14,960°, $[\Phi]_{262}$ +15,190°, $[\Phi]_{252}$ 0°, $[\Phi]_{284}$ −12,795°, $[\Phi]_{279}$ −7075°, and

(17) Melting points are corrected and were taken on a Fisher-Johns apparatus or a Thomas–Hoover capillary apparatus. Optical rotations were measured in chloroform solution at 27° and infrared spectra were determined in KBr discs unless otherwise specified. Ultraviolet spectra were measured on a Cary Model 14 spectrometer. We wish to thank Dr. L. Throop and his staff for these measurements. Pmr spectra were recorded for 5–10% solutions (w/v) in deuteriochloroform containing tetramethylsilane as internal reference on Varian A-60 and HA-100 spectrometers. Chemical shifts are reported as parts per million on the δ scale to the nearest 0.01 ppm. Coupling constants are reported in cycles per second to the nearest 0.5 Hz. We thank Mr. J. W. Murphy and Miss J. Tremble for assistance with these measurements. Mass spectra were obtained with an Atlas werke CH-4 spectrometer equipped with a direct inlet system. Spectra were measured at an ionizing potential of 70 eV and an acceleration voltage of 3 kV. We wish to thank Dr. L. Tökes and Mr. J. Smith for assistance with these measurements. Microanalyses were performed by Dr. A. Bernhardt, Mülheim (Ruhr), West Germany.

(18) D. Seyferth and J. M. Burlitch, *J. Organometal. Chem.*, **4**, 127 (1965).

(19) Preparative tlc was conducted using silica gels GF and HF (from Brinkmann Instruments, Inc., N. Y.) at thicknesses of 1.3 mm and steroid loadings of 2 mg/cm.

$[\Phi]_{208}$ 0°; λ_{max} 252 mμ (log ε 4.16); ν_{max} 1740, 1720, 1680, and 1250 cm^{-1}; nmr 0.70 (s, H-18), 1.11 (s, H-19), 2.03 (s, H-17α-acetoxy), 2.11 (s, H-21), and 6.14 ppm (s, H-4).

Anal. Calcd for $C_{24}H_{30}O_4Cl_2$: C, 63.57; H, 6.67; Cl, 15.64. Found: C, 63.50; H, 6.72; Cl, 15.70.

The 17 alcohol **10c** (50 mg) gave the following data: mp 259–260° (from acetone); $[\alpha]_D$ +107°; λ_{max} 251 mμ (log ε 4.09); ν_{max} 3460, 1710, 1670, and 1660 cm^{-1}; nmr 0.56 (s, H-18), 1.07 (s, H-19), 2.09 (s, H-21), and 6.00 ppm (s, H-4).

Anal. Calcd for $C_{22}H_{28}O_3Cl_2$: C, 64.23; H, 6.86. Found: C, 64.37; H, 6.91.

Reaction of 17α-Acetoxy-3,3-cycloethylenedioxypregna-4,6-dien-20-one (8c) with Phenyl(trichloromethyl)mercury.—A solution of **8c** (830 mg) and phenyl(trichloromethyl)mercury (950 mg) in benzene (210 ml) was heated under reflux for 120 hr. Since tlc analysis showed the presence of starting **8c**, an additional 950 mg of the mercurial reagent was added and the solution was boiled again for 72 hr. Purification of the crude product by preparative tlc afforded **10b** (360 mg), mp 188°, identical in all respects with a sample of **10b** obtained from the preceding experiment, and the ketal adduct **10d** (235 mg): mp 166–167° (from acetone–hexane); $[\alpha]_D$ +58°; ν_{max} 1740, 1720, and 1250 cm^{-1}; nmr 0.67 (s, H-18), 0.95 (s, H-19), 2.01 (s, H-17α-acetoxy), 2.06 (s, H-21), 4.01 (s, cycloethylenedioxy H), and 5.71 ppm (s, H-4).

Anal. Calcd for $C_{26}H_{34}O_5Cl_2$: C, 62.77; H, 6.89; Cl, 14.25. Found: C, 62.54; H, 7.16; Cl, 14.08.

Treatment of ketal **10d** with methanol containing concentrated hydrochloric acid for 15 min at room temperature furnished the Δ^4-3 ketone **10b**.

Registry No.—Phenyl(trichloromethyl)mercury, 3294-57-3; **2a**, 23367-44-4; **2c**, 23330-50-9; **3a**, 23367-45-5; **3b**, 23330-51-0; **5**, 23330-52-1; **9**, 23330-53-2; **10b**, 23157-28-0; **10c**, 23330-55-4; **10d**, 23330-56-5.

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Steroidal β-Lactams

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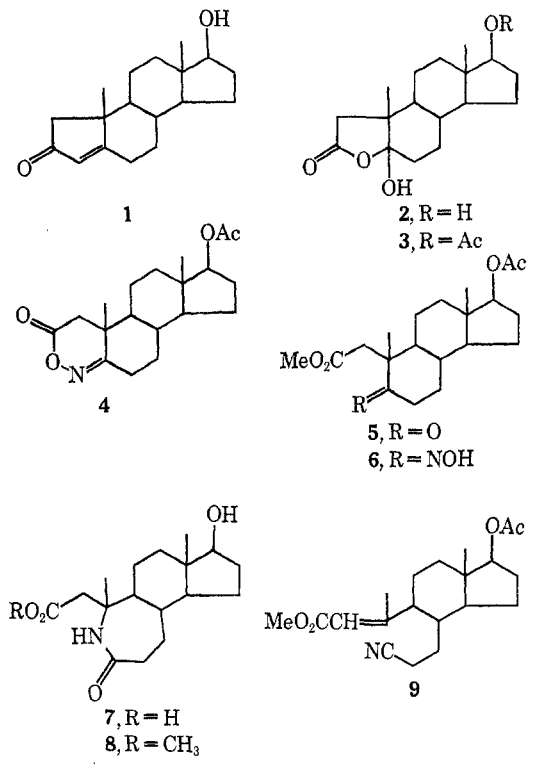
The multistep conversion of A-nortestosterone into a new B-homo steroidal ring system possessing a fused β-lactam as ring A is described. The deshielding effect of the nitrogen atom on the C-19 methyl signal in the nmr spectra of the 5-aza steroidal compounds prepared in this study is discussed briefly.

In this paper, the conversion of A-nortestosterone (**1**)[1] into a new steroidal ring system possessing a fused β-lactam as ring A[2] will be described.[3] The synthesis of this novel structure was of interest to us from both a chemical and biological point of view.

The synthetic scheme for the preparation of the steroidal β-lactam can be divided into three parts. The first stage involves the removal of a carbon atom from ring A of **1** to give a seco compound bearing a two-carbon side chain attached to C-10, the terminal carbon atom of the side chain being oxygenated. The next problem concerns the positioning of a nitrogen atom into ring B in a β relationship to the oxygen-bearing carbon atom of the side chain. Lastly, the modified steroid skeleton must be transformed into a β-amino acid that can then be cyclized to the β-lactam.

The removal of carbon atom 3 from **1** could be achieved by hydroxylation of the conjugated double bond with osmium tetroxide, followed by oxidative cleavage with periodic acid to afford the lactonol **2**.[4] Our synthesis required large amounts of **2**, and it was more conveniently prepared in one step by use of the periodate–permanganate combination.[5] Reaction of **2** with acetic anhydride in pyridine at room temperature resulted in selective acetylation at C-17 to give **3**. Acetylation of the hydroxyl at C-5 is possible, if this reaction is conducted at reflux temperature.

In our initial attempt to introduce the nitrogen atom into ring B in the form of an oxime, we treated **3** with hydroxylamine hydrochloride in pyridine at reflux temperature. The product did not exhibit any hydroxyl or carboxyl bands in the ir spectrum, but showed two carbonyl bands at 5.68 and 5.80 μ. This compound was assigned the cyclic structure **4**, which was confirmed by elemental analysis and the presence of an AB quartet at τ 7.26 and 7.76 (J = 16 cps) in the nmr spectrum for the C-1 methylene hydrogens. In order to circumvent the undesired cyclization of the oximino



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