Evidence that the bromine atom is at C_4 was provided by conversion of the bromoketone to the 2,4-dinitrophenylhydrazone of testosterone acetate, which formed reddish orange microcrystals from chloroform–methanol, m.p. 216–217°, λ^{EtOH} 385 mμ (29,800), negative Beilstein test; identity established by mixed m.p. and ultraviolet comparisons with an authentic sample[3] prepared from testosterone acetate.

4β-Bromotestane-3β,17β-diol 17-Acetate.—A mixture of 8.37 g. of 4β-bromotestane-17β-ol-3-one acetate, 1.2 g. of sodium borohydride and 100 cc. of absolute ethanol was let stand at 25° for 6 hr., diluted with water, extracted with ether, and the product adsorbed onto 200 g. of alumina from 20 cc. of 1:1 petroleum ether–benzene. Chromatography was conducted as in the above series and each fraction was crystallized from petroleum ether. Early eluates (petroleum ether–benzene: 200 cc. of 1:1, 300 cc. of 1:3, followed by 300 cc. of benzene) gave 2.13 g. of the 3β,4β-bromohydrin, m.p. 145–154°. On recrystallization to constant m.p. from aqueous methanol the substance was obtained as prisms (1.85 g.), m.p. 155–156°, α_D +72° Chf (*c* 2.41), λ^{Chf} 2.79, 5.79, 7.9, 10.34 μ.

Anal. Calcd. for $C_{21}H_{33}O_3Br \cdot H_2O$ (431.41): C, 59.82; H, 8.18. Found: C, 59.87; H, 7.92.

The acetate, crystallized from aqueous methanol, formed prisms, m.p. 164–165°, α_D +68° Chf (*c* 2.03).

Anal. Calcd. for $C_{23}H_{35}O_4Br$ (455.43): C, 60.65; H, 7.74. Found: C, 60.71; H, 7.94.

A mixture of 407 mg. of 4β-bromotestane-3β,17β-diol 17-acetate, 0.9 g. of potassium hydroxide and 15 cc. of methanol was heated under a stream of nitrogen to effect solution and let stand at 25° for 48 hr. The reaction product crystallized poorly from aqueous acetone to give impure testane-17β-ol-3-one, m.p. 138–139°, α_D +30° EtOH (*c* 1.17), no depression in mixed m.p. with authentic material, m.p. 142–143°. However, acetylation and crystallization from ether gave 178 mg. of prismatic plates of **testane-17β-ol-3-one acetate**, m.p. and mixed m.p. 145–146°.

Hydrogenation of 486 mg. of 4β-bromotestane-3β,17β-diol 17-acetate (245 mg. palladium–charcoal, 1 g. potassium hydroxide, 50 cc. 95% ethanol; complete in a few minutes) and crystallization of the product from ether–petroleum ether afforded in the first crop 127 mg. of **testane-3β,17β-diol**, m.p. 175–178°, λ^{Chf} 2.78, 2.9 μ, Beilstein test negative; recrystallized from ether–petroleum ether, m.p. 162–164°, α_D +15° EtOH (*c* 1.38). This material is solvated; on oxidation it gave **testane-3,17-dione**, m.p. and mixed m.p. 131–132°, α_D +103° Chf (*c* 2.21), λ^{Chf} 5.78, 5.86μ.

4β-Bromotestane-3α,17β-diol 17-acetate was isolated from late fractions of the above chromatogram; 200-cc. portions of 19:1, 9:1 and 4:1 benzene–ether eluates afforded, on crystallization from petroleum ether, a total of 2.85 g. of bromohydrin melting in the range 138–144°. Recrystallization from aqueous methanol gave prismatic needles, m.p. 143–144°, α_D +47° Chf (*c* 1.91), λ^{Chf} 2.79, 5.79, 7.95 μ.

The acetate formed prismatic needles from aqueous methanol, m.p. 164–165°, α_D +34° Chf (*c* 2.18); mixed m.p. with the 3β-epimer, 135–145°.

Intermediate chromatogram fractions (0.62 g.) seemed to consist of mixtures of the two bromohydrins, m.p. 130–132°, 137–139°, 138–145°. Ether–methanol (9:1) eluted **testane-3α,17β-diol 17-acetate**, which crystallized from ether as thin needles (20 mg.), m.p. 173–175°, λ^{Chf} 2.9, 5.79, 8.0 μ, negative Beilstein test. Acid hydrolysis gave testane-3α,17β-diol, m.p. (from methanol) and mixed m.p. 230–231°.

Treatment of 408 mg. of 4β-bromotestane-3α,17β-diol 17-acetate with methanolic potassium hydroxide as described above gave 155 mg. of crude **3α,4α-oxidotestane-17β-ol**, m.p. about 155°. Recrystallization from aqueous methanol gave small prisms, m.p. 157–159°, α_D +13° Chf (*c* 2.38) λ^{Chf} 2.77, 2.9 μ, Beilstein test negative.

Hydrogenation of 495 mg. of 4β-bromotestane-3α,17β-diol 17-acetate gave 166 mg. of crude **testane-3α,17β-diol**, m.p. 220–225°; twice recrystallized from methanol: m.p. 230–231°, α_D +26° EtOH (*c* 1.66).[4]

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(3) B. A. Koechlin, T. H. Kritchevsky and T. F. Gallagher, *J. Biol. Chem.*, **184**, 393 (1950).

(4) L. Ruzicka, M. W. Goldberg and W. Boshard, *Helv. Chim. Acta*, **20**, 541 (1937), report m.p. 236–236.5°, α_D +24.8° EtOH.

Compounds for Cancer Studies[1]

BY CARL TABB BAHNER, LEE ROY BARCLAY, GEORGE BIGGERSTAFF, DOROTHY ELLIS BILANCIO, GAY WALDEN BLANC, MARGUERITE CLOSE, MARY MARGUERITE ISENBERG AND EDWIN PACE

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The quaternary salts listed in Table I have been synthesized by the methods cited, for screening as potential antitumor agents.

TABLE I

QUATERNARY SALTS

Salt	Empirical formula	M.p., °C.	Ionic halogen, % Calcd.	Found
Methyl *p*-toluenesulfonate salt of Quinoxaline[a]	$C_{16}H_{16}N_2O_3S$	150	[b]	
Allyl bromide salt of Quinoxaline[a]	$C_{11}H_{11}BrN_2$	111	31.85	31.86
n-Propyl iodide salt of Quinoxaline[a]	$C_{11}H_{13}IN_2$	145	42.29	42.43
Methyl iodide salt of 2-(*p*-Acetylamino-styryl)-pyridine[c]	$C_{16}H_{17}IN_2O$	298	33.38	33.26
Decyl iodide salt of 4-(*p*-Dimethylamino-styryl)-pyridine[c]	$C_{25}H_{37}IN_2$	209	25.77	25.85
2,5-Diiodohexane salt of 3-Acetylpyridine[d]	$C_{20}H_{28}I_2N_2O_2$	222–225	43.76	43.78
3-Cyanopyridine[d]	$C_{18}H_{20}I_2N_4$	243	46.38	46.30
Iodoacetonitrile salt of γ-Picoline	$C_8H_9IN_2O$	169	48.80	48.51
p-Fluorophenacyl bromide salt of Lepidine[e]	$C_{18}H_{16}BrFNO$	218	22.19	22.04
4-Methyl-5-(β-hydroxyethyl)-thiazole[f]	$C_{14}H_{15}BrFNO_2S$	209	22.19	22.28
β-Naphthacyl bromide salt of 4-Methyl-5-(β-hydroxyethyl)-thiazole[f]	$C_{18}H_{18}BrNO_2S$	213	20.39	20.20
2,5-Dichlorophenacyl bromide salt of Hexamethylene-tetramine[g]	$C_{14}H_{17}BrCl_2N_4O$	174	19.58	19.52

[a] C. T. Bahner and Wm. K. Easley, THIS JOURNAL, **72**, 3803 (1950). [b] Calcd.: C, 60.74; H, 5.09. Found: C, 60.86; H, 5.25. We are indebted to the National Cancer Institute for carbon and hydrogen analyses. [c] C. T. Bahner, E. S. Pace and Robert Prevost, *ibid.*, **73**, 3407 (1951). [d] C. T. Bahner, Wm. K. Easley, M. D. Pickens, H. D. Lyons, L. L. Norton, B. G. Walden and G. E. Biggerstaff, *ibid.*, **73**, 3499 (1951). [e] C. T. Bahner, Wm. K. Easley, B. G. Walden, H. D. Lyons and G. E. Biggerstaff, *ibid.*, **74**, 3960 (1952). [f] C. T. Bahner, Donald Pickens and D. B. Bales, *ibid.*, **70**, 1652 (1948). [g] C. T. Bahner, M. D. Pickens, Donald Pickens and Wm. K. Easley, *ibid.*, **72**, 3266 (1950.)

The fact that quaternary salts of hexamethylenetetramine are unstable in aqueous solution has raised the question whether the biological effects of such solutions[2] are due to products derived from the salts within the blood stream. Since it is known that under certain conditions quaternary hexamethylenetetraminium salts form amines[3] or aldehydes,[4] a number of amines and aryl glyoxals which might be formed from the corresponding salts have been synthesized in order to determine whether they would have the same activity against sarcoma cells as the quaternary salts. Active compounds were found among all three types.

Among the aryl glyoxals prepared by selenium

(1) This research was supported in part by a research grant from the National Institutes of Health, U. S. Public Health Service, and in part by a grant from the Damon Runyon Memorial Fund for Cancer Research.

(2) C. T. Bahner, M. D. Pickens, D. Pickens and W. K. Easley, THIS JOURNAL, **72**, 2266 (1950).

(3) T. Immediata and A. R. Day, *J. Org. Chem.*, **5**, 512 (1940).

(4) Sommelet, *Compt. rend.*, **157**, 852 (1913).

dioxide oxidation of the corresponding methyl ketones[5] was the new compound *p*-fluorophenylglyoxal hydrate, white crystals, decomposing at 93–94°.

Anal. Calcd. for $C_8H_7FO_3$: C, 56.65; H, 4.13. Found: C, 56.80; H, 4.57.

We are indebted to Dr. M. J. Shear and Dr. J. L. Hartwell of the National Cancer Institute, and Dr. Louis H. Goodson of Midwest Research Institute, and their associates for suggestions and for arranging screening tests.

(5) A. H. Blatt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 509.

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The Steric Configuration of Brominated 3-Ketosteroids[1]

BY R. NORMAN JONES

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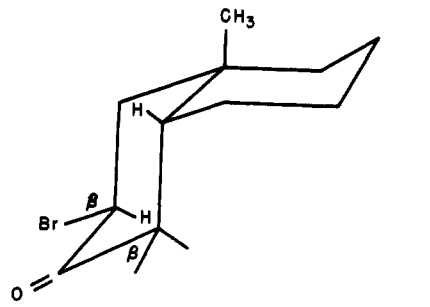
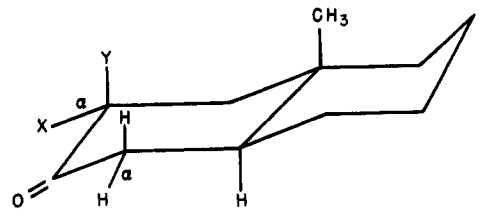
To explain the effects of vicinal bromination on the C=O stretching band in the infrared spectra of ketosteroids, it was postulated[2] that when the C—Br and C=O bonds are coplanar the frequency of the carbonyl band is increased by 15–20 cm.$^{-1}$, but when the C—Br and C=O bonds are perpendicular, bromination does not change the frequency of this band. This observation was subsequently confirmed by Corey who has generalized it to other cyclic α-haloketones.[3]

For the chair conformations I and II conventionally assigned to the A rings of normal and allo-3-ketosteroids, a positive frequency shift should occur on bromination at the equatorial C_2- and C_4-positions, and on this basis the configurations 4β-bromocoprostan-3-one and 2α-bromocholestan-3-one were predicted.[2] The 4β-bromocoprostan-3-one structure has been substantiated by Fieser and Dominguez[4] on the basis of chemical evidence. These investigators assigned a 2β-configuration to 2-bromocholestan-3-one, but Fieser and Wei-Yuan Huang[5] now regard this compound as 2α-bromocholestan-3-one, in accord with spectrographic considerations.

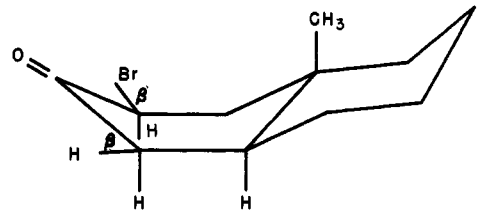
The validity of the general assumption of a chair conformation for ring A in allo-steroids has been questioned by Fieser and Dominguez.[4] In assigning the bromine configurations spectrographically this assumption was specifically made and it is the object of this note to draw attention to the fact that if 2β-bromo-3-ketoallosteroids have a boat conformation IV the C—Br bond will be coplanar with the C=O bond and the conditions for a positive carbonyl frequency shift will be satisfied. It is therefore to be anticipated that the position of the C=O stretching band will fail to distinguish between 2α-bromocholestan-3-one in the conventional chair configuration, and 2β-bromocholestan-3-one in the boat configuration IV.



I



II X = Br Y = H
III X = H Y = Br



IV

There can be little doubt that the non-halogenated 3-ketoallosteroids will possess the stabler chair structure, but in the 2β- and 4β-bromo derivatives the bromine atoms approach closely to the C_{19} angular methyl group in the chair form and repulsion between these groups may be sufficient to stabilize the boat structure.

Although at present it is not possible to differentiate between boat and chair conformations of ring A by infrared spectroscopy, the carbonyl absorption strongly suggests that these vicinal bromo-ketones must exist predominantly or exclusively in one conformation only. A labile equilibrium of the type III ⇄ IV should reveal itself by a broadening, asymmetry or doubling of the carbonyl band. Although such an effect has been looked for it has not been observed.

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(1) Published as Contribution No. 3060 from the Laboratories of The National Research Council of Canada.

(2) R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1952).

(3) E. J. Corey, *ibid.*, **75**, 2301 (1953).

(4) L. F. Fieser and X. A. Dominguez, *ibid.*, **75**, 1704 (1953).

(5) L. F. Fieser and Wei-Yuan Huang, *ibid.*, **75**, 4837 (1953).

Platinum–Olefin Compounds

BY BODIE E. DOUGLAS

RECEIVED APRIL 3, 1953

Chatt[1] and Chatt and Wilkins[2] reviewed the various structures which have been proposed for olefin coördination compounds and reasons for rejecting each of these were presented. The ob-

(1) J. Chatt, *J. Chem. Soc.*, 3340 (1949).

(2) J. Chatt and R. G. Wilkins, *Nature*, **165**, 859 (1950).