The author wishes to express his deepest thanks to Prof. Takeo Ueda for the kind leading in these studies.

Summary

In order to find antimicrobial agents, the substitution of 3-acetamido-6-alkoxypyridazine 2-oxide was investigated. As the results obtained, it was made clear that a number of 3-acetamido-6-alkoxypyridazine, 3-amino-6-alkoxypyridazine and their 2-oxides having such a substituent group as nitro, amino, hydroxyamino, azo, hydrazo, chloro, methoxy, methylthio, hydroxy, and mercapto at 5-position of the pyridazine rings, were synthesized. This finding is of use to develope the chemistry of pyridazine.

Among these new compounds, 3-acetamido- and 3-amino-5-nitro-6-alkoxypyridazine 2-oxides were found to exert excellent *in vitro* effects on pathogenic bacteria.

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UDC 577.17[547.92]

190. Kikuo Yasuda : Oxidation of 3-Enol Derivatives of 4-En-3-oxo-steroids by *tert*-Butyl Chromate.

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Several works[1] on *t*-butyl chromate oxidation of steroids, especially 3β-acetoxy- and 3-ethylenedioxy-Δ^5-steroids to the corresponding 7-ones have been carried out, since Oppenauer and Oberrauch[2] reported on the oxidation of cholesteryl acetate. There has been, however, no report on *t*-butyl chromate oxidation of 3-enol derivatives of 4-en-3-oxo-steroids, although Fieser obtained 6β-hydroxycholest-4-en-3-one by sodium dichromate oxidation of cholest-4-en-3-one enol acetate.[3] Some observations on *t*-butyl chromate oxidation of such derivatives are described in the present paper.*2

When testosterone enol diacetate (Ia) was oxidized with *t*-butyl chromate in the presence of acetic anhydride, there was obtained the corresponding 7-one (IIa). The structure of IIa was confirmed because the same substance was given by acetylation of 3,17β-dihydroxyandrosta-3,5-dien-7-one 17-acetate (Va), which was prepared from 3-ethylenedioxy-17β-acetoxyandrost-5-en-7-one (VIa) by the method of Marshall and his coworkers.[4] Their assignment of structure (Va) was based upon analogy to 3-hydroxycholesta-3,5-dien-7-one[5] for which, however, the possibility of another enolic form, 7-hydroxycholesta-4,6-dien-3-one, was suggested. Now this possibility can be evidently excluded from the above-mentioned observation. IIa (UV : λ_{max} 282 mμ) was treated

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*1 1604, Shimosakunobe, Kawasaki (安田喜久男).

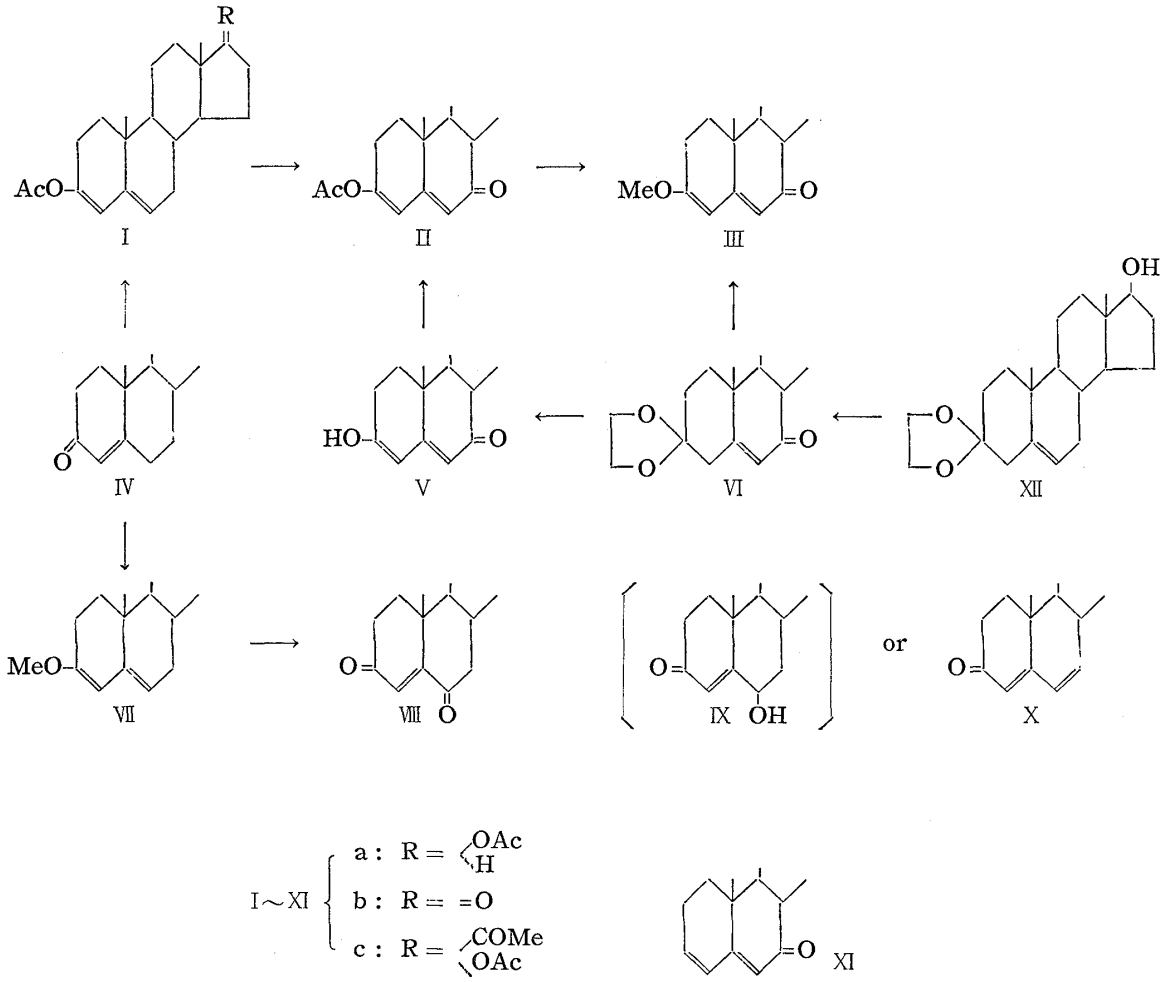
*2 Presented in part at the 14th Annual Meeting of the Pharmaceutical Society of Japan (1961).

1) Most recently : E. Menini, J.K. Norymbergsky : Biochem. J., **84**, 195 (1962) (on 3β-hydroxy-5-enes and 4-en-3-ones).
2) R.V. Oppenauer, H. Oberrauch : Ann. Asoc. Quim. Argentina, **37**, 246 (1949) (C.A., **44**, 3871 (1950)).
3) L.F. Fieser : J. Am. Chem. Soc., **75**, 4377 (1953).
4) C.W. Marshall, R.E. Ray, I. Laos, B. Riegel : *Ibid.*, **79**, 6303 (1957).
5) *a*) J. Barnett, B.E. Ryman, F. Smith : J.Chem. Soc., **1946**, 526. *b*) C.W. Greenhalgh, H.B. Henbest, F.R.H. Jones : *Ibid.*, **1952**, 2375.

with aqueous methanolic sulfuric acid to give the corresponding 3-methyl ether (IIIa) (UV : λ_{max} 311 mμ), which was also obtained by treatment of VIa with the same reagent.

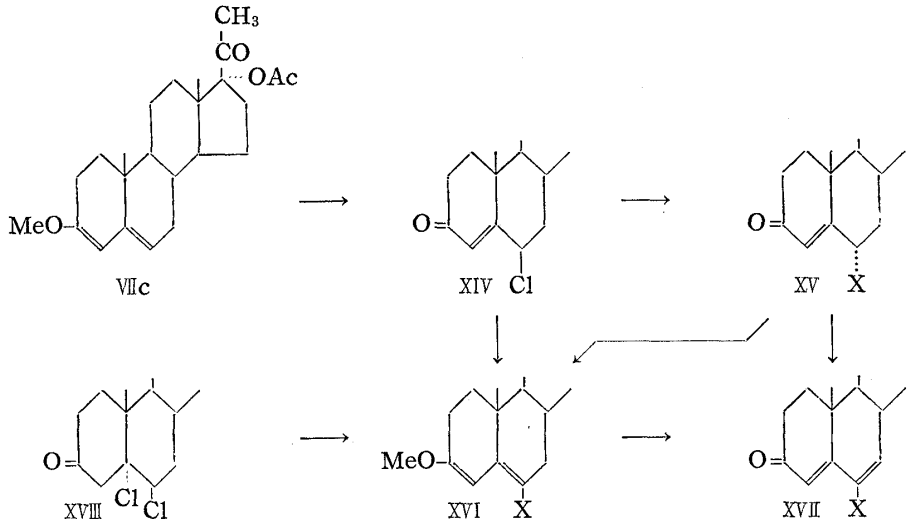
Similar transformations of 3-enol acetates of androst-4-ene-3,17-dione (IVb) and 17α-acetoxyprogesterone (IVc) were performed.

Enol methyl ethers were oxidized under three different conditions as follows; i) at room temperature without acetic anhydride; ii) at 5~10° without acetic anhydride; iii) at a higher temperature (50~60°) in the presence of acetic anhydride. The 3-enol methyl ethers described below were readily prepared by treatment of the corresponding 4-en-3-ones with methyl orthoformate and *p*-toluenesulfonic acid in dioxane. When 3-methoxyandrosta-3,5-diene-17β-ol acetate (VIIa) was oxidized at room temperature, the main product was 17β-acetoxyandrost-4-ene-3,6-dione (VIIIa) (accompanied by a small amount of 17β-acetoxyandrosta-4,6-dien-3-one), and at 5~10°, 6β,17β-dihydroxyandrost-4-en-3-one 17-acetate (IXa) was obtained as the main crystalline product. These compounds were identified by comparison with the authentic samples.[6,7] Similar results were obtained in the oxidation of 3-methoxyandrosta-3,5-dien-17-one (VIIb) and 3-methoxy-17α-acetoxypregna-3,5-dien-20-one (VIIc) at room temperature. On the oxidation of VIIb and VIIc at 5~10°, attempts to obtain the corresponding 6β-ols crystalline were unsuccessful, but infrared and ultraviolet spectra of the reaction products showed the presence of considerable amounts of 6β-ols.



6) H. Mori : This Bulletin, **9**, 328 (1961).
7) J. Romo, G. Rosenkranz, C. Djerassi, F. Sondheimer : J. Org. Chem., **19**, 1509 (1954).

Treatment of VIIa at a higher temperature in the presence of acetic anhydride afforded 17β-acetoxyandrsta-4,6-dien-3-one (Xa). The corresponding 4,6-dien-3-ones, Xb and Xc, were also obtained by similar oxidation of VIIb and VIIc, respectively. The structures of 4,6-dien-3-ones were approved by ultraviolet spectra and comparison with the authentic samples prepared from the corresponding 4-en-3-ones (IV) by chloranil oxidation.[8]



XVa, XVIa and XVIIa : X= -Cl
XVb, XVIb and XVIIb : X= -Me

TABLE I. Ultraviolet (in MeOH) and Infrared (in $CHCl_3$) Absorptions of XI, II and III

Type of A and B ring / Type of D ring	XI ν_{max} cm^{-1} $7_{C=O}$	XI Δ^3 & Δ^5	XI λ_{max} mμ ($\varepsilon\times10^4$)	II ν_{max} cm^{-1} $7_{C=O}$	II Δ^3 & Δ^5	II λ_{max} mμ ($\varepsilon\times10^4$)	III ν_{max} cm^{-1} $7_{C=O}$	III Δ^3 & Δ^5	III λ_{max} mμ ($\varepsilon\times10^4$)
a	1651	1594 1623	279 (2.33)	1639	1598 1660[a]	282 (2.44)	1604	1561[a] 1648	311 (2.63)
b	1650	1594 1624	279 (2.17)	1639	1600 1660[a]	282 (2.34)	1608	1560[a] 1642	311 (2.73)
c	1655	1598 1626	279 (2.06)	1640	1600 1661[a]	282 (2.33)	1608	1561[a] 1650	311 (2.55)
Mean	1652	1595 1626	279 (2./10)	1639	1599 1660[a]	282 (2.37)	1607	1561[a] 1648	311 (2.64)

a) Inflection

8) *a*) F.J. Agnello, G.D. Laubach : J. Am. Chem. Soc., **79**, 1257 (1957). *b*) *Idem* : *Ibid.*, **82**, 4293 (1960). *c*) J.A. Campbell, J.C. Babcock : *Ibid.*, **81**, 4072 (1959). *d*) H.J. Ringold, E. Batres, A. Bowers, J. Edwards, J. Zderic : *Ibid.*, **81**, 3485. *e*) H.J. Ringold, J.P. Ruelas, E. Batres, C. Djerassi : *Ibid.*, **81**, 3715.

As 6-chloro- and 6-methyl-17α-acetoxypregna-4,6-diene-3,20-dione (XVIIa and XVIIb)[9] possess surprisingly high progestational activities, it is quite important to establish a practical method of preparation. 3-Methoxy-6-chloro-17α-acetoxypregna-3,5-dien-20-one (XVIa) was obtained from 6β-chloro- or 6α-chloro-17α-acetoxyprogesterone (XIV or XVa) by the same enolmethylation described above. XVIa was also obtained from 17α-acetoxy-5α,6β-dichloropregnane-3,20-dione (XVIII)*3 by one step of similar treatment (under reflux). XVIa was converted into XVIIa by *t*-butyl chromate oxidation in a considerably high yield. 6α-Methyl-17α-acetoxyprogesterone (XVb) was similarly transformed into XVIIb *via* the corresponding 3-enol methyl ether (XVIb).

It is reported[5b,11] that in the ultraviolet absorpion of cholesta-3,5-dien-7-one an acetoxy and a methoxy group at C_3 exert a 6 mμ and a 31 mμ shift, respectively. An analogous relationship was observed in the infrared and ultraviolet spectral data of 3-acetoxy-3,5-dine-7-ones (II), 3-methoxy-3,5-dien-7-ones (III) and 3,5-dien-7-ones (XI)*4 (Table I andFig. 1).

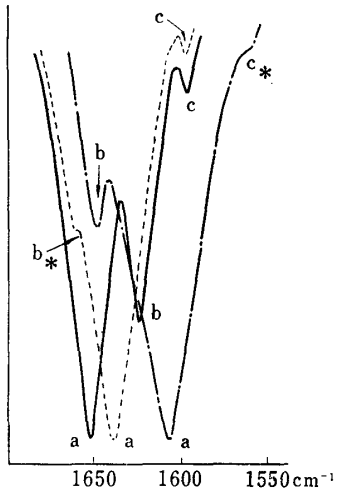


Fig. 1. Schematic Intrared Spectra of XI, II and III (in $CHCl_3$)

——— XI
····· II
—·—·— III

a : $7_{C=O}$
b, c : Δ^3 and Δ^5
* : Inflection

Experimental*7

General Procedures

1) ***t*-Butyl Chromate Oxidation at Room Temperature**——To a solution of an enol methyl ethyl ether (VII) (1 part) in CCl_4 (10 parts) was dropwise added *t*-butyl chromate in CCl_4 solution[12] (10 parts) with stirring over a period of 10 min. at room temperature. After 2 hr. oxalic acid (3 parts) in H_2O (20 parts) was added to the reaction mixture. After 1 hr. the whole was extracted with $CHCl_3$ and the extract was washed with H_2O, dried over anhyd. Na_2SO_4, passed through Florisil and evaporated under reduced pressure. The residue was recrystallized from a suitable solvent.

2) ***t*-Butyl Chromate Oxidation in the Presence of Acetic Anhydride**——A solution of an enol acetate (I) or an enol methyl ether (VII) (1 part) in CCl_4 (30 parts) was heated with *t*-butyl chromate in CCl_4 solution (10 parts) and Ac_2O (1 part) at 50~60° for 4 hr., and then the reaction mixture was treated as described above.

3) **Chloranil Oxidation**[8c]——A solution of a 4-en-3-one (IV) (1 part) in Me_2CO (20 parts) was refluxed with chloranil (1 part) for 2 hr., then concentrated to about 0.1 volume over a period of 1 hr., diluted with Et_2O, washed with 4% NaOH, H_2O, dried over anhyd. Na_2SO_4 and evaporated. The residue was recrystallized from a suitable solvent.

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*3 Prepared by Dr. J. Yamada, *et al.* in this Laboratory and will be published elsewhere shortly.
*4 Prepared by the method of Marshall, *et al.*[10]
*7 Melting points are uncorrected. Rotations were measured in $CHCl_3$ and UV spectra in MeOH.

9) A. Zaffaroni : Acta Endocrinologica, Supplementum, **50** (accompanies Vol., **34**), 139 (1960).
10) C. W. Marshall, R. E. Ray, I. Laos, B. Riegel : J. Am. Chem. Soc., **79**, 6308 (1957).
11) L. Dorfman : Chem. Revs., **53**, 80 (1953).
12) K. Heusler, A. Wettstein : Helv. Chim. Acta, **35**, 289 (1952).

4) **Hydrolysis with aq, Methanolic Sulfuric Acid**——A solution of a ketal (VI) or an acetate (II) (1 part) in MeOH (100 parts) was gently refluxed with 10% H_2SO_4 (5 parts) for 30 min., then evaporated without further heating to about 0.1 volume under reduced pressure and poured into H_2O. The precipitates were collected, washed with H_2O, dried and subjected to recrystallization and chromatography, suitably combined.

5) **Acetylation of Dienolones (V)**——To a solution of a dienolone (V) (1 part) in pyridine (5 parts) was added Ac_2O (3 parts) at room temperature. After 1 hr. the reaction mixture was poured into H_2O. The precipitates were collected, washed with H_2O, dried and recrystallized from a suitable solvent.

6) **Enolmethylation**——A mixture of a 4-en-3-one (IV, XIV or XV) (1 part), dry dioxane (5 parts), methyl orthoformate (1 part) and *p*-TsOH·H_2O (0.04 part) was stirred for 1 hr. at 50~60°, then cooled to room temperature and diluted with H_2O (about 10 parts) containig pyridine (about 0.5 part). The precipitates were collected after stirring 1 hr., washed with H_2O, dried and recrystallized from a suitable solvent.

3,17β-Diacetoxyandrosta-3,5-dien-7-one (IIa)

a) From Ia——The residue resulting from 650 mg. of Ia by procedure (2) (not at 50~60° but under reflux) was recrystallized from MeOH to 190 mg. of IIa, m.p. 217~220°. Repeated recrystallization from the same solvent afforded an analytical sample as colorless fine needles, m.p. 223~225°. $[\alpha]_D^{20}$ −238° (c=0.66), UV : λ_{max} 282 mμ (ε 23,400). *Anal.* Calcd. for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found : C, 71.61; H, 7.82.

b) From Va——25 mg. of Va was treated by procedure 5). Two recrystallizations of the resulting precipitates from MeOH gave 17 mg. of IIa, m.p. 218~221°, which was identical with the acetate obtained above.

3-Acetoxyandrosta-3,5-dien-7,17-dione (IIb)

a) From 3-Acetoxyandrosta-3,5-dien-17-one (Ib)——A mixture of androst-4-ene-3,17-dione (IVb) (10 g.), dry benzene (40 ml.), isopropenyl acetate (10 ml.) and *p*-TsOH·H_2O (0.5 g.) was refluxed for 30 min., then evaporated slowly and finally under reduced pressure almost to dryness and diluted with H_2O. The precipitates were collected, washed with 5% Na_2CO_3, H_2O, dried and recrystallized from MeOH (containing a few drops of pyridine) to 8.3 g. of Ib, m.p. 127~131°. Repeated recrystallization from the same solvent furnished an analytical sample as colorless needles, m.p. 130~133°, $[\alpha]_D^{20}$ −80° (c=0.72), UV : λ_{max} 234 mμ (ε 17,500) (in the lit.,[13] m.p. 127~129°). *Anal.* Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found : C, 76.68; H, 8.63.

1 g. of Ib (m.p. 127~131°) was treated by procedure (2) (under reflux). The resulting residue was chromatographed on Florisil with benzene to 170 mg. of IIb, m.p. 195~205°, from the earlier eluents. Repeated recrystallization from Me_2CO afforded an analytical sample as colorless scales, m.p. 208~211°, $[\alpha]_D^{20}$ −245° (c=0.99), UV : λ_{max} 282 mμ (ε 24,400). *Anal.* Calcd. for $C_{21}H_{26}O_4$: C, 73.66; H, 7.66. Found : C, 73.62; H, 7.36.

b) From 3-Hydroxyandrosta-3,5-diene-7,17-dione (Vb)——The precipitates obtained from 30 mg. of Vb by procedure (5) were recrystallized from Me_2CO to 230 mg. of IIb, m.p. 204~209°, which was identical with the acetate obtained above.

3,17-Diacetoxypregna-3,5-diene-7,20-dione (IIc)

a) From 3,17α-Diacetoxypregea-3,3-dien-20-one (Ic)——The residue resulting from 1.7 g. of Ic (m.p. 198~203°) by procedure (2) (under reflux) was recrystallized from Me_2CO to 510 mg. of bulky yellow needles, m.p. 194~203°, UV : λ_{max} 282 mμ (ε 20,000). Two recrystallizations from Me_2CO gave 240 mg. of IIc, m.p. 217~221°. Further recrystallization afforded an analytical sample as colorless thin plates, m.p. 217.5~219°, $[\alpha]_D^{20}$ −391° (c=0.24), UV : λ_{max} 282 mμ (ε 23,300). *Anal.* Calcd. for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53. Found : C, 70.46; H, 7.34.

130 mg. of Xc (m.p. 219~221°) was obtained from the mother liquors after laborious recrystallization.

b) From 3,17α-Dihydroxypregna-3,5-diene-7,17-dione 17-Acetate (Vc)——33 mg. of Vc was treated by procedure (5). The resulting precipitates were recrystallized from Me_2CO to colorless scales, m.p. 217~219°, which were identical with IIc obtained above.

Oxidation of 3-Methoxyandrosta-3,5-dien-17β-ol Acetate (VIIa)

a) By Procedure (1)——The residue resulting from 1 g. of VIIa by procedure (1) was recrystallized from Et_2O to 230 mg. of VIIIa as yellow prisms, m.p. 195~200°, which was identical with an authentic sample.[6] Chromatography of the mother liquors on Florisil afforded a small amount of Xa, m.p. 137~142° (from MeOH), from the earlier eluents with benzene-hexane (1:1).

b) By Procedure (1) at 5~10°——1 g. of VIIa was treated by procedure (1) not at room temperature but at 5~10°. Recrystallization of the resulting residue from Me_2CO-hexane gave 200 mg. of IXa as colorless needles, m.p. 204~207°. One more recrystallization from Me_2CO furnished an analytical

13) L. Ruzicka, W.H. Fiescher : Helv. Chim. Acta, **19**, 1371 (1936).

sample, UV : λ_{max} 234 mμ (ε 16,100), which was identical with an authentic sample prepared from Ia by the method of Romo, *et al.*[7]

c) By Procedure (2)——The residue resulting from 1 g. of VIIa by procedure (2) was recrystallized from MeOH to 250 mg. of Xa as colorless needles, m.p. 135~137°, UV : λ_{max} 283 mμ (ε 24,100), which was identical with an authentic sample prepared from testosterone acetate (IVa) by procedure (3).

Oxidation of 3-Methoxyandrosta-3,5-dien-17-one (VIIb)

a) By Procedure (1)——The residue resulting from 1 g. of VIIb by procedure (1) was recrystallized from MeOH to 311 mg. of androst-4-ene-3,6,17-trione (VIIIb) as yellow prisms, m.p. 206~212°. Two recrystallizations from the same solvent afforded an analytical sample, m.p. 218~220°, UV : λ_{max} 252 mμ (ε 10,000), which was identical with an authentic sample.[14] Chromatography of the mother liquors on Florisil with benzene gave a small amount of androsta-4,6-diene-3,17-dione (Xb), but attempts to detect 6β-hydroxyandrost-4-ene-3,17-dione (IXb) were unsuccessful.

b) By Procedure (2)——The residue resulting from 1 g. of VIIb by procedure (2) was recrystallized from MeOH to 190 mg. of Xb, m.p. 166~171°. One more recrystallization from MeOH gave an analytical sample as colorless prisms, m.p. 169~173°, UV : λ_{max} 284 mμ (ε 25,400), which was identical with a sample prepared from androst-4-ene-3,17-dione (IVb) by procedure (3).

Oxidation of 3-Methoxy-17α-acetoxypregna-3,5-dien-20-one (VIIc)

a) By Procedure (1)——The residue resulting from 1 g. of VIIc by procedure (1) was recrystallized from MeOH to 210 mg. of 17α-acetoxypregn-4-ene-3,6,20-trione (VIIIc) as slightly yellow needles, m.p. 211~215°, which was identical with an authentic sample.[6]

b) By Procedure (2) under Reflux——1 g. of VIIc was treated by procedure (2) not at 50~60° but under reflux. Recrystallization of the resulting residue from MeOH gave 260 mg. of Xc, m.p. 208~214°. Repeated recrystallization from the same solvent furnished an analytical sample as colorless prisms, m.p. 220.5~221.5°, $[\alpha]_D^{24}$ +12° (c=1.00), UV : λ_{max} 282~284 mμ (ε 23,400). *Anal.* Calcd. for $C_{23}H_{30}O_4$: C, 74.56 : H, 8.16. Found : C, 74.27; H, 8.14.

Chloranil Oxidation of IVc——The residue resulting from 5 g. of IVc by procedure (3) was recrystallized from MeOH to 2.4 g. of Xc as slightly yellow prisms, m.p. 214~218°, which was identical with the dienone obtained above.

17α-Acetoxy-6-chloropregna-4,6-diene-3,20-dione (XVIIa)——5 g. of XVIa was treated by procedure (2) (9 hr. reflux). The resulting residue was stirred with Et_2O (15 ml.) for 1 hr. The precipitates were collected, washed with Et_2O and recrystallized from Me_2CO to 2.1 g. of XVIIa as pale yellow prisms, m.p. 206~209°, UV : λ_{max} 286 mμ (ε 23,500), which was identical with an authentic sample prepared from XVa by chloranil oxidation in EtOAc with AcOH.*8,8d)

6-Methyl-17α-acetoxypregna-4,6-diene-3,20-dione (XVIIb)——2.5 g. of XVIb was treated by procedure (2) (4.5 hr. reflux). The resulting residue was recrystallized from Me_2CO-hexane to 630 mg. of XVIIb, m.p. 207~212°. Repeated recrystallization gave an analytical sample as colorless cubes, m.p. 215~217°, UV : λ_{max} 288 mμ (ε 21,900), which was identical with an authentic sample prepared from XVb by chloranil oxidation with AcOH.[8e]

3-Methoxy-17β-acetoxyandrosta-3,5-dien-7-one (IIIa)

a) From VIa——Recrystallization of the precipitates resulting from 50 mg. of VIa[4] by procedure (4) gave 15 mg. of IIIa, m.p. 257~260°. Repeated recrystallization from MeOH-Me_2CO afforded an analytical sample as colorless needles, m.p. 263~266°, $[\alpha]_D^{20}$ −320° (c=0.50), UV : λ_{max} 311 mμ (ε 27,300). *Anal.* Calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found : C, 73.80; H, 8.06.

b) From IIa——The precipitates resulting from 100 mg. of IIa by procedure (4) were recrystallized from MeOH-Me_2CO to 43 mg. of IIIa, m.p. 256~261°, which was identical with the Me_2O obtained above.

3-Methoxyandrosta-3,5-diene-7,17-dione (IIIb)

a) From 3-Ethylenedioxyandrost-5-ene-7,17-dione (VIb)——5 g. of 3-ethylenedioxyandrost-4-en-17β-ol (XIII) was treated by procedure (2). Recrystallization of the resulting residue from Me_2CO gave 3.1 g. of VIb, m.p. 173~183°. Repeated recrystallization from the same solvent afforded an analytical sample as colorless cubes, m.p. 187~189°, $[\alpha]_D^{20}$ −16° (c=1.02), UV : λ_{max} 241 mμ (ε 13,800). *Anal.* Calcd. for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19. Found : C, 73.41; H, 8.53.

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*8 The method of Ringold, *et al.* resulted in a very low yield and attempts to raise the yield were all in vain. Although Agnello and Laubach reported[8b] that an enol ether was oxidized more rapidly than the corresponding 4-en-3-one with chloranil, no significant difference was observed in this case.

14) A. Butenandt, B. Riegel : Ber., **69**, 1163 (1936); K. Tsuda, H. Iizuka, Y. Sato, M. Naito : This Bulletin, **9**, 925 (1961).

500 mg. of VIb (m.p. 173~183°) was treated by procedure (4). The resulting precipitates were chromatographed on Florisil with benzene to 230 mg. of IIIb, m.p. 202~205°, from the later eluents. Repeated recrystallization from Me_2CO furnished an analytical sample as needles, m.p. 206~207°, UV: λ_{max} 311 mμ (ε 26,300), which was identical with an authentic sample.[15] *Anal.* Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.03; H, 8.42.

b) From IIb——The precipitates resulting from IIb (50 mg.) by procedure (4) were recrystallized from MeOH to 200 mg. of IIIb, m.p. 205~207°, which was identical with the Me_2O obtained above.

3-Methoxy-17α-acetoxypregna-3,5-diene-7,20-dione (IIIc)

a) From 3-Ethylenedioxy-17α-acetoxypregn-5-ene-7,20-dione (VIc)——The precipitates resulting from VIc[4] (300 mg.) by procedure (4) were recrystallized from MeOH to 70 mg. of IIIc, m.p. 249~253°. Two recrystallizations from the same solvent gave an analytical sample as colorless needles, m.p. 252~254°, $[\alpha]_D^{20}$ −357° (c=0.61), UV: λ_{max} 311 mμ (ε 25,500). *Anal.* Calcd. for $C_{24}H_{32}O_5$: C, 71.97; H, 8.05. Found: C, 71.70; H, 7.59.

b) From IIc——IIc (50 mg.) was treated by procedure (4). Recrystallization of the resulting precipitates from MeOH gave 17 mg. of IIIc, m.p. 246~251°, which was identical with the Me_2O obtained above.

3-Methoxy-6-chloro-17α-acetoxypregna-3,5-dien-20-one (XVIa)

a) From XIV——A mixture of VII (10 g.), Me_2CO (300 ml.), NaOAc (2 g.) and H_2O (10 ml.) was stirred with NCS (5.5 g., 1.5 mol. equivalent as 100% NCS) at room temperature for 1 hr., and poured into H_2O. The precipitates were collected, washed with H_2O, dried and recrystallized from Me_2CO-hexane to 8.9 g. of crude XIV,[8d] m.p. 211~214°.

5 g. of the crude XIV was treated by procedure (6). The resulting precipitates were recrystallized from Me_2CO (containing a few drops of pyridine) to 4.7 g. of XVIa, m.p. 225° (decomp.). Repeated recrystallization from the same solvent afforded an analytical sample as colorless scales, m.p. 232~233 (decomp.), $[\alpha]_D^{28}$ −127° (c=1.65), UV: λ_{max} 251 mμ (ε 22,700). *Anal.* Calcd. for $C_{24}H_{33}O_4Cl$: C, 68.47; H, 7.90. Found: C, 68.55; H, 7.98.

XVa[8d] was also converted into XVIa in similar yield by procedure (6).

b) From XVIII——A mixture of XVIII[3] (m.p. 171~173° (decomp.)) (1 g.), dry dioxane (10 ml.), methyl orthoformate (1 ml.) and *p*-TsOH·H_2O (40 mg.) was refluxed for 1 hr., then cooled to room temperature and poured into H_2O (100 ml., containing 0.5 ml. of pyridine). The precipitates were treated as described above to give 710 mg. of XVIa, m.p. 223° (decomp.), which was identical with the Me_2O obtained above.

Enolmethylations of other 4-en-3-ones, IVa, IVb, IVc and XVb, were listed in Table II.

Table II. Enolmethylations of 4-En-3-ones by Procedure (6)

Starting meterial	Recryst. solvent[a]	Yield of VII	Physic. const.[b] of anal. sample	Analysis		
IVa (10 g.)	Et_2O-MeOH	8.8 g. m.p. 173~178°	m.p. 176~180°, $[\alpha]_D^{21}$ −152° (c=1.00) UV: λ_{max} 238 mμ (ε 22,800)	Cald. for $C_{22}H_{32}O_3$	C 76.70	H 9.36
				Found	76.16	9.09
IVb (10 g.)	MeOH	6.3 g. m.p. 161~171°	m.p. 170~174°, $[\alpha]_D^{21}$ −89° (c=1.00) UV: λ_{max} 238 mμ (ε 24,000)	Cald. for $C_{20}H_{28}O_2$	C 79.95	H 9.30
				Found	79.97	9.48
IVc (10 g.)	〃	8.5 g. m.p. 190~194°	m.p. 195~198°,[c] $[\alpha]_D^{21}$ −151° (c=1.00) UV: λ_{max} 238 mμ (ε 23,200)	Cald. for $C_{24}H_{34}O_4$	C 74.37	H 8.87
				Found	74.58	8.81
XVb (1.5 g.)	〃	1.3 g. m.p. 205~220°	m.p. 217~222°, $[\alpha]_D^{28}$ −176° (c=0.39) UV: λ_{max} 249 mμ (ε 18,300)	Cald. for $C_{25}H_{36}O_4$	C 74.96	H 9.06
				Found	74.71	9.24

a) Containing a few drops of pyridine.
b) Rotations were measured in $CHCl_3$ containing pyridine[e] (2 drops/10 ml.).
c) In the most recent lit.,[d] m.p. 195~198°, $[\alpha]_D^{25}$ −135° (1% pyridine in $CHCl_3$), UV: λ_{max} 239 mμ (ε 21,000).
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Summary

3-Enol acetates of some 4-en-3-oxo-steroids were oxidized to the corresponding 7-ones with *t*-butyl chromate and 3-enol methyl ethers were to the corresponding 4-ene-3,6-diones, 6β-hydroxy-4-en-3-ones or 4,6-dien-3-ones according to the reaction conditions. 3-Enol methyl ethers were prepared with methyl orthoformate in dioxane by catalysis of *p*-toluenesulfonic acid. 17α-Acetoxy-5α,6β-dichloropregnane-3,20-dione was converted into 3-methoxy-6-chloro-17α-acetoxypregna-3,5-dien-20-one in one step.

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191. Shoji Shibata,[*1] Akihiro Ohta,[*2] and Yukio Ogihara[*1] : Metabolic Products of Fungi. XXI.[*3] On Ustilaginoidins. (1).[*4] The Reactions of Ustilaginoidin A.

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An optically active red coloring matter named ustilaginoidin was isolated from the false smutted ball (*Ustilaginoidea virens* (Cooke) Takahashi[1]) growing parasitically on spike of rice plant (in Japanese—Inekoji (稲麹)).

Yabuta and Sumiki and their coworkers[2] proposed a molecular formula, $C_{19}H_{16}O_7$, for ustilaginoidin and assumed that it belongs to the anthraquinone pigment mainly on the basis of obtaining anthracene on zinc dust distillation. However, the earlier study of ustilaginoidin was interrupted without providing further evidences for the structure.

In relation to some other studies on the fungal anthraquinones we realized a fact that ustila ginoidin gave no characteristic color reactions of hydroxyanthraquinone, which prompted us to reexamine its chemical structure.

The acetone extracts of the false smutted ball (*Ustilaginoidea virens*) collected from the infected rice spikes were separated by $CaHPO_4$-column chromatography to give three bands. The lowest band which consisted the main portion of the extracts was eluted and recrystallized from dioxan to give a red pigment m.p. >300°, $[\alpha]_D$ −384°, which would correspond to ustilaginoidin of earlier workers and now has been designated ustilaginoidin A.

Ustilaginoidin A recrystallized from dioxan gave analytical figures and molecular weight (determined by X-ray crystallographical method) consistent with $C_{28}H_{18}O_{10}\cdot 2C_4H_8O_2$, which lost dioxan on drying at 180° *in vacuo*. It is slightly soluble in bicarbonate solution and soluble in carbonate to formed solution. It gives a red color in conc. H_2SO_4, which turns into green on heating. It shows a green color with $FeCl_3$ and no remarkable coloration with magnesium acetate in alcohol.

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