large number of 1,5-diaryl-2,3-pyrrolidinediones has been synthesized, and several curious aspects of their chemical behavior have been studied in this laboratory.[2-6]

Previous evidence to the contrary notwithstanding,[4,7] we now wish to report conclusive proof that the structures of such compounds have been incorrectly assigned. Addition of *p*-anisidine to β-(*p*-methoxybenzoyl)-acrylic acid affords α-(*p*-anisylamino)-β-(*p*-methoxybenzoyl)-propionic acid, m.p. 144.5–145.0° dec.

Anal.[8] Calc'd for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.80; N, 4.25. Found: C, 65.69; H, 5.79; N, 4.25.

Treatment of this ketoacid with sodium borohydride, followed by benzoyl chloride in pyridine yielded α-(N-benzoyl-*p*-anisylamino)-γ-*p*-anisyl-γ-butyrolactone, m.p. 164.5–165.5°.

Anal.[8] Calc'd for $C_{25}H_{23}NO_5$: C, 71.95; H, 5.55; N, 3.36. Found: C, 71.82; H, 5.53; N, 3.37.

This substance was shown by identity of infrared spectra and mixture melting point determination to be identical with the benzoyl derivative of the cyclic reduction product obtained by Vaughan and Peters[3] by catalytic hydrogenation and benzoylation of β-(*p*-anisylidine)-α-(*p*-anisylimino)-propionic acid (IIb), reacting as its proved cyclic tautomer, then presumed to be Ib, 1,5-dianisyl-2,3-pyrrolidinedione (enol form).

The absorption band in the high frequency range of the infrared spectra of substances previously held to be the enolic forms of 1,5-diaryl-2,3-pyrrolidinediones[7] is now assigned to N—H rather than O—H, since the treatment of Ia with sodium nitrite in glacial acetic acid affords an N-nitroso derivative whose infrared spectrum is transparent in the N—H region. The nitroso compound melts with decomposition at 216.0–216.5°.

Anal.[8] Calc'd for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 10.00. Found: C, 68.71; H, 4.17; N, 10.14.

The original substance thus has an endocyclic double bond which is evidently in the α,β-position (as in an enamine form), since the carbonyl absorption at 1736 cm.$^{-1}$ is at a lower frequency than is that for the dihydrolactone (1742 cm.$^{-1}$), whereas it would be at a higher frequency than in the dihydrolactone, if the double bond were β,γ.[9]

The present evidence for the structure of Ia and Ib coupled with the striking similarity in infrared spectra[7] and chemical behavior[2-4] as well as methods of synthesis,[7] for all previously reported and otherwise unsubstituted 1,5-diaryl-2,3-pyrrolidinediones constitutes a reasonable basis for assigning to all such compounds the 5-aryl-3-arylamino-2(5H)-furanone (V) structure.[10] Thus there is no available evidence for the existence of the otherwise unsubstituted 1,5-diaryl-2,3-pyrrolidinedione system,[11] and the previously reported reaction, I ⇄ II, becomes a special case of lacto-enoic tautomerism:[12] V ⇄ II.

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(2) W. R. Vaughan and L. R. Peters, *J. Org. Chem.*, **18**, 393 (1953).

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(4) W. R. Vaughan and D. I. McCane, *J. Org. Chem.*, **20**, 143 (1955).

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(6) W. R. Vaughan, *J. Org. Chem.*, **20**, 1619 (1955).

(7) W. R. Vaughan and L. R. Peters, *J. Org. Chem.*, **18**, 382 (1953).

(8) Spang Microanalytical Laboratories, Ann Arbor, Michigan.

(9) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 160.

(10) This structure is the enamine form of the α-iminolactone proposed by K. Garzarolli-Thurnlackh [*Monatsh.*, **20**, 480 (1899); *Ber.*, **32**, 2274 (1899)] and was suggested to one of us (W.R.V.), along with a similar interpretation of our published infrared data[7] and the present type of structure proof, in 1953 by Dr. J. A. King in a private communication.

(11) It should be emphasized that this disproof of structure does not in any way apply to 2,3-pyrrolidinediones with 4-substituents or to the simpler 1-substituted compounds, for which conclusive structural evidence is available.

(12) R. P. Linstead and H. N. Rydon, *J. Chem. Soc.*, 580 (1933).

(13) National Science Foundation Predoctoral Fellow, 1954–1957.

Steroids. LXXXIV.[1] Synthesis of 6-Methyl Hormone Analogs

Sir:

The recent communication[2] describing the preparation of 6α-methyl cortical hormone analogs prompts us to announce at this time the synthesis of a number of 6-methyltestosterone and progesterone derivatives some of which possess potentiated biological activity. Perbenzoic acid oxidation of Δ^5-androstene-3β,17β-diol diacetate and reaction of the resulting 5α,6α-oxide (m.p. 165–166°, $[\alpha]_D$ −71°. Found: C, 70.65; H, 9.08[3]) with methylmagnesium bromide in ether-benzene gave 6β-methylandrostane-3β,5α,17β-triol (I)[4] (m.p. 137–138°, $[\alpha]_D$

(1) Paper LXXXIII, H. J. Ringold and G. Rosenkranz, *J. Org. Chem.*, in press.

(2) Spero, Thompson, Magerlein, Hanze, Murray, Sebek, and Hogg, *J. Am. Chem. Soc.*, **78**, 6213 (1956).

(3) All melting points are uncorrected. Rotations were determined at 20° in chloroform and ultraviolet absorption spectra in 95% ethanol.

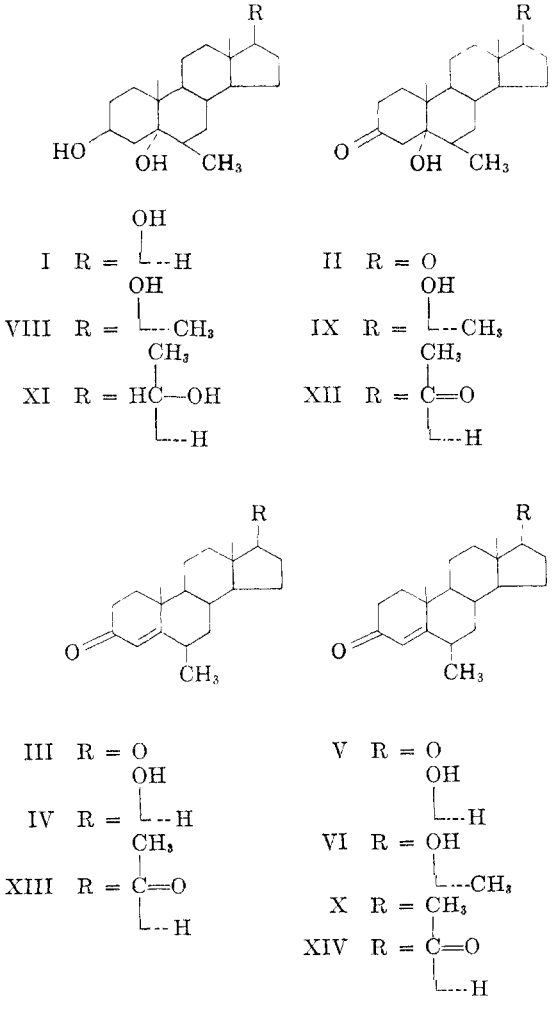
(4) Ushakov and Madaeva, *J. Gen. Chem.* (U.S.S.R.), **9**, 436 (1939), first observed the opening of cholesterol α-oxide with methylmagnesium iodide. Turner, *J. Am. Chem. Soc.*, **74**, 5363 (1952) investigated this reaction further and prepared 6α- and 6β-methylcholestone from the Grignard reaction product.

$-8°$)[5] which was oxidized with pyridinium chromate to 6β-methylandrostan-5α-ol-3,17-dione (II) (m.p. 228–230°, $[\alpha]_D$ +77°. Found: C, 75.16; H, 9.37). Thionyl chloride–pyridine dehydration of II at 0° yielded 6β-methyl-Δ^4-androstene-3,17-dione (III) (m.p. 175–176°, $[\alpha]_D$ +132°, λ_{max} 242 mμ, log ε 4.19. Found: C, 79.96; H, 9.52) from which 6β-methyltestosterone (IV) (m.p. 209–210°, $[\alpha]_D$ +48°, λ_{max} 242 mμ, log ε 4.19. Found: C, 79.32; H, 10.14) was derived by lithium aluminum hydride reduction followed by manganese dioxide oxidation.[6] Treatment of II with methanolic potassium hydroxide, resulting in dehydration and methyl inversion, yielded 6α-methyl-Δ^4-androstene-3,17-dione (V) (m.p. 168–170°, $[\alpha]_D$ +176°, λ_{max} 240 mμ, log ε 4.21. Found: C, 80.02; H, 9.35) which was converted to 6α-methyltestosterone (VI) (m.p. 158–159°, $[\alpha]_D$ +91°, λ_{max} 242 mμ, log ε 4.20. Found: C, 79.60; H, 10.02) by sodium borohydride reduction.[7] The latter was also readily obtained from IV by acidic or alkaline inversion of the 6β-methyl (axial) group. Catalytic hydrogenation of IV over a palladium-carbon catalyst gave almost exclusively the allo derivative 6β-methylandrostan-17β-ol-3-one (VII) (m.p. 203–205°, $[\alpha]_D$ +37°. Found: C, 79.26; H, 10.65).

Similarly, 17α-methyl-Δ^5-androstene-3β,17β-diol 3-acetate was converted to the 5,6α-oxide (m.p. 164–165°, $[\alpha]_D$ −84°. Found: C, 72.76; H, 9.09), thence to 6β,17α-dimethylandrostane-3β,5α,17β-triol (VIII) (m.p. 191–192°, $[\alpha]_D$ −45°)[5] by means of methylmagnesium bromide, to 6β,17α-dimethylandrostane-5α,17β-diol-3-one (IX) (m.p. 253–254°, $[\alpha]_D$ −26°. Found: C, 75.36; H, 10.43) by pyridinium chromate oxidation, and 6α,17α-dimethyltestosterone (X) (m.p. 136–137°, $[\alpha]_D$ +71°, λ_{max} 242 mμ, log ε 4.19. Found: C, 79.49; H, 10.09) finally derived from IX by methanolic alkali treatment.

The readily available Δ^5-pregnene-3β,20β-diol diacetate served as starting material for the preparation of 6α- and 6β-methylprogesterone by a reaction scheme essentially identical to that described above and involving the following intermediates: 5α,6α-oxidoallopregnane-3β,20β-diol diacetate (m. p. 180–181°, $[\alpha]_D$ −39°. Found: C, 71.58; H, 9.11), 6β-methylallopregnane-3β,5α,20β-triol (XI) (m.p. 236–237°, $[\alpha]_D$ −31°. Found: C, 75.22; H, 10.69), 6β-methylallopregnan-5α-ol-3,20-dione (XII) (m.p. 264–265°, $[\alpha]_D$ +75°. Found: C, 76.13; H, 9.75). Thionyl chloride-pyridine dehydration of XII led to 6β-methylprogesterone (XIII) (m.p. 170–172°, $[\alpha]_D$ +135°, λ_{max} 242 mμ, log ε 4.21. Found: C, 80.16; H, 9.65) while alkaline treatment of XII or XIII gave the stable (equatorial) isomer 6α-methylprogesterone (XIV) (m.p. 119–121°, $[\alpha]_D$ +177°, λ_{max} 242 mμ, log ε 4.21. Found: C, 80.40; H, 9.95).

In the immature castrate male rat (subcutaneous administration) 6α-methyltestosterone (VI) exhibits 0.9× the androgenic (measured by the prostate and seminal vesicles) and 4.6× the myotrophic (levator ani muscle) potency of testosterone.[8] 6β-Methyldihydrotestosterone (VII) is 3.9× as androgenic and 8.1× as myotrophic as testosterone in the same test. In the guinea pig copulatory assay[8] both 6β- and 6α-methylprogesterone (XIII and XIV) exhibit an order of activity slightly greater than the parent progesterone.



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(5) Satisfactory carbon-hydrogen analyses could not be obtained for I and VIII apparently due to solvent of crystallization.

(6) *Cf.* Sondheimer, Amendolla, and Rosenkranz, *J. Am. Chem. Soc.*, **75**, 5930 (1953).

(7) *Cf.* Norymberski and Woods, *J. Chem. Soc.*, 3426 (1955).

(8) Bioassays by the Endocrine Laboratories, Madison, Wis.