Anal. Found: C, 29.35, 29.45; H, 6.86, 6.92; N (Dumas), 9.21; $SO_4^=$ (as barium sulfate), 28.26, 28.44.

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STEROIDS. II.[1] A METHOD FOR THE CONVERSION OF *ALLO*-STEROIDS INTO Δ^4-3-KETOSTEROIDS

Sir:

The current interest in corticosteroids as possible therapeutic agents in arthritis has made the availability of starting materials extremely important. Since the majority of the *abundant* steroidal plant sapogenins, representing a potentially unlimited source for 20-keto-pregnanes, either belong to the *allo* series or possess a Δ^5-3-hydroxy grouping, which in turn is convertible in nearly quantitative yield into the 3-keto*allo*steroid system (I), it has become an urgent matter to develop a general procedure for the transformation of I into the essential Δ^4-3-keto moiety.

We have observed that while 3-keto-4-bromosteroids of the *normal* series (rings A/B *cis*) do not react with sodium iodide in acetone solution, 2-bromo-3-keto*allo*steroids (rings A/B *trans*) readily react to yield the corresponding iodo derivatives, which on treatment with zinc dust in ethanol, chromous chloride in acetone, or even short *boiling with collidine* regenerate the saturated 3-keto*allo*steroids. When applied to 2,4-dibromo-3-keto*allo*steroids (II), obtainable in high yield from I, short boiling with sodium iodide affords a 2-iodo-4-bromo-3-keto*allo*steroid (*e. g.*, 2-iodo-4-bromoandrostan-17-ol-3-one 17-hexahydrobenzoate, m. p. 146–149°. Calcd. for $C_{26}H_{38}O_3BrI$: C, 51.58; H, 6.33. Found: C, 51.71; H, 6.35), which on refluxing with collidine suffers simultaneous dehydrobromination and deiodination to lead directly to the required Δ^4-3-ketosteroid. Even more strikingly, if II is refluxed with sodium iodide in acetone solution for twenty hours, there is obtained in good yield a 2-iodo-Δ^4-3-ketosteroid (III), which is smoothly transformed to the Δ^4-3-ketosteroid. The generality of this method has already been demonstrated in five diverse instances in this Laboratory and will be exemplified here by the preparation of the important adrenal hormone 17α-hydroxyprogesterone.

N-Bromoacetamide oxidation of *allo*pregnane-3β,17α-diol-20-one[2] gave a high yield of *allo*pregnan-17α-ol-3,20-dione (IV) (m. p. 251–253°, $[\alpha]^{20}D$ + 24°), which on dibromination in acetic acid led to the 2,4-dibromo derivative (V) (m. p. 183–185° $[\alpha]^{20}D$ 0°. Calcd. for $C_{21}H_{30}O_3Br_2$: C, 51.44; H, 6.17. Found: C, 51.64; H, 5.88). Twenty hours of refluxing with sodium iodide in acetone yielded 2-iodo-17α-hydroxyprogesterone (m. p. 112–115°, $[\alpha]^{20}D$ + 71°, maximum 244 mμ (log E 4.15). Calcd. for $C_{21}H_{29}O_3I$: I, 27.81. Found: I, 28.32), which without isolation on deiodination afforded 17α-hydroxyprogesterone (VI) (m. p. 220–222°, $[\alpha]^{20}D$ + 103° (acetone), maximum 241 mμ (log E 4.30)). The present method, in addition to ready availability of starting materials and good yields, has the marked advantage over the corresponding *normal* ketones in that from each saturated 3-keto*allo*steroid (*e. g.*, IV), three unsaturated ketones of interest for clinical trial can be prepared: in addition to VI, V on collidine treatment afforded the interesting $\Delta^{1,4}$-pregnadien-17α-ol-3,20-dione (m. p. 232–234°, $[\alpha]^{20}D$ + 38.5°, maximum 244 mμ (log E 4.14). Calcd. for $C_{21}H_{28}O_3$. C, 76.79; H, 8.59. Found: C, 76.96; H, 8.21), while the monobromination product of IV on dehydrobromination yielded the Δ^1-isomer of VI, Δ^1-allopregnen-17α-ol-3,20-dione (m. p. 254–257°, $[\alpha]^{20}D$ + 71°, maximum 230 mμ (log E 4.05). Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.49; H, 9.33).

Details, applications and extension of this method to other cortical hormones and analogs will be reported shortly.

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(1) Paper I, THIS JOURNAL, **71**, 3689 (1949).

(2) Kritchevsky and Gallagher, *J. Biol. Chem.*, **179**, 507 (1949).

NITROGEN FIXATION IN AN ULTRASONIC FIELD

Sir:

Our observations on the oxidative fixation of molecular nitrogen in ultrasonic field have led to results which are of special interest in the connection of biological nitrogen fixation.

The experiments were carried out in water solution at ordinary pressure; radiating surface of the vessel was 42 mm. in diameter; radiation intensity in the radiation point was ~10 W/sq. cm., frequency 300 kc./sec. The hydrogen and nitrogen gases were led to the other side of the solution at the rate of about 1 l./min., carbon monoxide gas 0.4 l./min. Thus, oxygen was present in the solution in each experiment.

The nitrogen fixation in ultrasonic field does not, at least essentially, depend on the hydrogen ion concentration of the solution as far as the total amount of fixed nitrogen, nitrite *plus* nitrate N (other N-compounds have not been found), is considered. On the other hand, the mutual relation of nitrite and nitrate N is decided by the *p*H of the solution (Figs. 1 and 2). These results explain the observation of Loiseleur[1] on the rapid

(1) Loiseleur, *Compt. rend.*, **218**, 876 (1944).