Full details of the work on the two species mentioned will be reported later.

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(11) M. Pailer and A. Schleppnik, *Monatsh.*, **88**, 367 (1957).

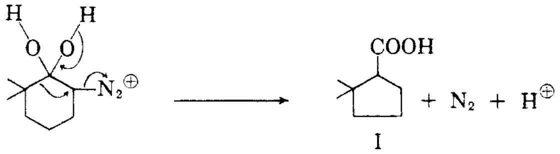
Deamination of α-Aminoketones

Sir:

Observation that nitrous acid deamination of a primary aminoketone derived from the alkaloid lycoctonine[1] gave an acid led us to consider the possibility that aliphatic α-aminoketones would give acids by Favorskii-type rearrangement on deamination.

We have now shown that 2-aminocyclohexanone hydrochloride[2] (prepared by stannous chloride reduction of 2-oximinocyclohexanone) gives up to 57% yields of carboxylic acid when treated with aqueous nitrous acid. This proved to be mainly cyclopentanecarboxylic acid (amide m.p. 179°; anilide, m.p. 165°, showing no melting point depression with authentic derivatives). Similarly, 2-amino-6,6-dimethylcyclohexanone (hydrochloride m.p. 182°, *Anal.*, Calcd. for $C_8H_{16}ONCl$: C, 54.08; H, 9.07; N, 7.82. Found: C, 53.47; H, 9.00; N, 7.92) gave a 25% yield of acid. This was mainly a saturated monocyclic acid $C_8H_{14}O_2$ (anilide, m.p. 125°, *Anal.*, Calcd. for $C_{14}H_{19}ON$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.49; H, 8.57; N, 6.44) which on mechanistic grounds and by analogy to the product from 2-aminocyclohexanone should be 2,2-dimethylcyclopentanecarboxylic acid (I). This assignment was supported by its infrared spectrum, which had the pair of peaks characteristic of a *gem*-dimethyl group (ν_{max} 1370 and 1385 cm.$^{-1}$, liquid film), and by the NMR spectrum of its methyl ester, which had two unsplit methyl signals at 186 and 199 c.p.s. (60 Mc, water reference). In addition, the spectrum contained signals due to a single hydrogen with a large chemical shift flanked by one methylene (triplet with J = 6.5 c.p.s. centered about +118 c.p.s.).

We suggest that the positive charge on the amine salt and diazonium ion aid hydration of the carbonyl, and that I is formed by the following mechanism:



I

Close analogs are found in the deamination of cyclic α-aminoalcohols[3] and the silver ion initiated rearrangement of α-bromoketones.[4]

Attempts to prepare I by vigorous alkaline treatment of 2-chloro-6,6-dimethylcyclohexanone (m.p. 62°, ν_{max} 1720 cm.$^{-1}$ as Nujol mull. *Anal.*, Calcd. for $C_8H_{13}OCl$: C, 59.81; H, 8.15; Cl, 22.07. Found: C, 59.65; H, 8.09; Cl, 22.33) and by the action of silver nitrate in aqueous alcohol[4] on 2-bromo-6,6-dimethylcyclohexanone (m.p. 58°. *Anal.*, Calcd. for $C_8H_{13}OCl$: C, 46.84; H, 6.38. Found: C, 47.05; H, 6.26) failed to yield more than traces of carboxylic acid. Hence the above deamination may prove a useful alternative to the Favorskii reaction when one carbon alpha to the carbonyl is quaternary.[5] The neutral products of the reaction are under investigation.

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[1] Unpublished work by O.E.E.

[2] H. E. Baumgarten and F. A. Bower, *J. Am. Chem. Soc.*, **76**, 4561 (1954).

(3) G. E. McCasland, *J. Am. Chem. Soc.*, **73**, 2293 (1951); D. Y. Curtin and S. Schmukler, *J. Am. Chem. Soc.*, **77**, 1105 (1955).

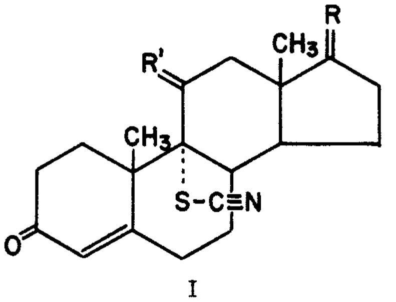
(4) A. C. Cope and E. S. Graham, *J. Am. Chem. Soc.*, **73**, 4702 (1951).

(5) R. B. Loftfield, *J. Am. Chem. Soc.*, **73**, 4707 (1951).

Synthesis of 9α- and 11β-Thiocyano Steroid Analogs

Sir:

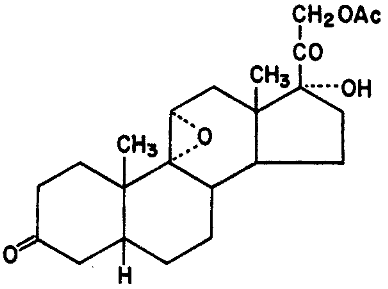
With the intention of finding antimetabolites of steroidal hormones, some thiocyano derivatives of corticoids and androgens (Ia–f and IIIa–b) have been synthesized.



I

(a) R = α-OH, -CO—CH_2OH
R′ = β-OH, -H
(b) R = α-OH, -CO—CH_2OAc
R′ = β-OH, -H
(c) R = =O
R′ = β-OH, -H
(d) R = α-OH, -CO—CH_2OH
R′ = =O
(e) R = α-OH, -CO—CH_2OAc
R′ = =O
(f) R= =O
R′ = =O

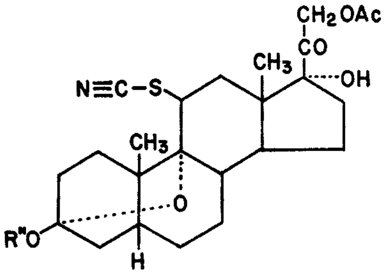
9β,11β-Oxido-Δ^4-pregnene-17α,21-diol-3,20-dione, its 21-acetate and 9β,11β-oxido-Δ^4-androstene-3,17-dione with hydrogen thiocyanide solution in acetic acid gave, respectively, 9α-thiocyano-Δ^4-pregnene 11β,17α,21-triol-3,20-dione (Ia) (yield *ca.* 28%), m.p. 174–175° (dec.), $[\alpha]_D^{20}$ +283.3° (dioxane), λ_{max}^{EtOH} 243 mμ (ε, 13,430), λ_{max}^{Nujol} 4.64μ (S—C≡N) (*Anal.* Calcd. for $C_{22}H_{29}O_5NS$: C, 62.98; H, 6.97; N, 3.34; S, 7.64. Found: C, 63.21: H, 7.16; N, 3.41; S, 7.65), its 21-acetate (Ib) (yield *ca.* 55%), m.p. 149–153° (dec.), $[\alpha]_D^{20}$ +224.9° (dioxane), λ_{max}^{EtOH} 243 mμ (ε, 14,000), λ_{max}^{Nujol} 4.66μ (S—C≡N) (*Anal.* Calcd. for $C_{24}H_{31}O_6NS$: C, 62.45: H, 6.77; N, 3.04; S, 6.95. Found: C, 62.43; H, 6.84; N, 3.25; S, 6.72) and 9α-thiocyano-Δ^4-androstene-11β-ol-3,17-dione (Ic) (yield *ca.* 35%), m.p. 160–162° (dec.), $[\alpha]_D^{20}$ +248.1° (dioxane), λ_{max}^{EtOH} 242 mμ (ε, 14,200), λ_{max}^{Nujol} 4.67μ (S—C≡N) (*Anal.* Calcd. for $C_{20}H_{25}O_3NS$: C, 66.82; H, 7.01; N, 3.90; S, 8.92. Found: C, 66.72; H, 7.16; N, 4.03; S, 8.44).



II

The chromic acid oxidation of Ib and Ic gave the corresponding 11-oxo compounds, 9α-thiocyano-Δ^4-pregnene-17α,21-diol-3,11,20-trione 21-acetate (Ie) (with one mol. of methanol of crystallization) (yield *ca.* 64%), m.p. 218–219° (dec.), $[\alpha]_D^{20}$ +333.7° (chloroform), +322.8° (dioxane), λ_{max}^{EtOH} 238 mμ (ε, 16,310), λ_{max}^{Nujol} 4.64μ (S—C≡N) (*Anal.* Calcd. for $C_{24}H_{29}O_6NS \cdot CH_3OH$: C, 61.08; H, 6.77; N, 2.85; S, 6.52; OCH_3, 6.31. Found: C, 61.22; H, 6.84; N, 2.87; S, 6.55; OCH_3, 6.12), and 9α-thiocyano-Δ^4-androstene-3,11,17-trione (If) (yield *ca.* 76%), m.p. 214–216° (dec.), $[\alpha]_D^{20}$ +453.6° (dioxane), λ_{max}^{EtOH} 236 mμ (ε, 14,270), λ_{max}^{Nujol} 4.64μ (S—C≡N) (*Anal.* Calcd. for $C_{20}H_{23}O_3NS$: C, 67.20; H, 6.49; N, 3.92; S, 8.97. Found: C, 66.97; H, 6.38; N, 4.28; S, 9.00). 9α-Thiocyano-Δ^4-pregnene-17α,21-diol-3,11,20-trione (Id), m.p. 245–246° (dec.), $[\alpha]_D^{20}$ +337.2° (dioxane), λ_{max}^{EtOH} 238 mμ (ε, 16,200), λ_{max}^{Nujol} 4.63μ (S—C≡N) (*Anal.* Calcd. for $C_{22}H_{27}O_5NS$: C, 63.29; H, 6.52; N, 3.36; S, 7.68. Found: C, 63.37; H, 6.53; N, 3.38; S, 7.62), was obtained in *ca.* 58% yield by hydrolysis of the 21-acetate (Ie) with hydrogen chloride in chloroform and methanol.

The reaction product of 9α,11α-oxido-5β-pregnane-17α,21-diol-3,20-dione 21-acetate (II),[1] m.p. 231–234°, $[\alpha]_D^{20}$ +30.0° (chloroform) (*Anal.* Calcd. for $C_{23}H_{32}O_6$: C, 68.29; H, 7.97. Found: C, 68.56; H, 8.13), with hydrogen thiocyanide solution when crystallized from acetone-hexane gave 3α,9α-oxido-11β-thiocyano-5β-pregnane-3β,17α,21-triol-20-one 21-acetate (IIIa) (yield *ca.* 65%), m.p. 155–156° (dec.), $[\alpha]_D^{20}$ +144.4° (chloroform), λ_{max}^{Nujol} 4.62μ (S—C≡N) (*Anal.* Calcd. for $C_{24}H_{33}O_6NS$: C, 62.18; H, 7.18; N, 3.02; S, 6.92. Found: C, 62.07; H, 7.19: N, 3.03; S, 6.96), when the reaction product was crystallized from methanol the 3-methylether (IIIb)[2] resulted (yield *ca.* 36%), m.p. 181–182°, $[\alpha]_D^{20}$ +120.1° (chloroform), λ_{max}^{Nujol} 4.63μ (S—C≡N) (*Anal.* Calcd. for $C_{25}H_{35}O_6NS$: C, 62.87; H, 7.39; N, 2.93; S, 6.71; OCH_3, 6.50. Found: C, 62.85; H, 7.54; N, 3.11; S, 6.58; OCH_3, 6.79).



III
(a) R″ = H
(b) R″ = CH_3

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(1) Prepared by catalytic reduction of the corresponding Δ^4-compound, J. Fried and E. F. Sabo, *J. Am. Chem. Soc.*, **79**, 1130 (1957). See also A. J. Lemin and C. Djerassi, *J. Am. Chem. Soc.*, **76**, 5672 (1954).

(2) *Cf.* H. Heymann and L. F. Fieser, *J. Am. Chem. Soc.*, **73**, 5252 (1951).

(3) Visiting Scientist (1957–59), National Institutes of Health.