In an alternate preparation of this diamine, a solution containing ethyl β-cyanobutyrate[3] (12 g.; b.p. 66° at 1 mm., $n^{25}D$ 1.4195), dimethylamine (16 g.) and ethanol (100 ml.) was heated in a bomb tube at 105° for 5 days. The N,N-dimethyl-β-cyanobutyramide (7.25 g., b.p. 77–78° at 5 mm;. $n^{25}D$ 1.4620) so prepared was reduced with excess lithium aluminum hydride (10 g.) in ether (600 ml.). 1-Amino-4-dimethylamino-2-methylbutane (3 g., b.p. 106–108° at 100 mm.) was isolated.[4] Its dioxalate (m.p. 175–176°) was the same as that of the diamine derived from the pyridazinium bromide (infrared spectra identical).

The ion ($R_2N{=}NH^+$) is probably the intermediate that reacts with the isoprene rather than the neutral species ($R_2N^+{=}N^-$) obtained when the reaction mixture is neutralized. The above pyridazinium salt was obtained (84% yield) directly from the acidic reaction mixture. When an acid solution from oxidation of 1,1-dimethylhydrazine and concentrated base were added simultaneously to a solution of isoprene in methanol at such rates that the reaction mixture remained just basic to phenolphthalein, tetramethyltetrazene (84% yield) was obtained.

Evidence that this intermediate reacts with aniline, phenol, styrene and vinyl *n*-butyl ether has been gained from experiments in which acid solutions of it were mixed with each of these substances (1–2 hour reaction times), and little or no tetramethyltetrazene was found by spectroscopic analysis after the reaction mixtures were made basic. The products here formed and further possible reactions are under investigation.

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RECEIVED NOVEMBER 2, 1957

ISOLATION AND SYNTHESIS OF A NEW STEROL FROM RAT FECES[1,2]

Sir:

In previous reports,[3,4] the presence of a new sterol (I) in rat feces was announced. Separation from the less polar coprostanyl *p*-phenyl azobenzoate was effected by chromatography of the mixed esters on silicic acid:Celite (2:1)[5] columns using petroleum ether (b.p., 90–95°). Saponification of (I) *p*-phenyl azobenzoate, and crystallization of the ensuing sterol (I) from absolute ethanol yielded thin needles; m.p. 146–147°, $[\alpha]^{25}D$ 0.00 in chloroform (*Anal.* Calcd. for $C_{28}H_{48}O$: C, 84.00; H, 12.00. Found: C, 83.35; H, 12.11). The infrared spectrum indicated absorptions at all the wave lengths believed to be characteristic of a Δ^7-stenol,[6] and the rate of color development with the Liebermann–Burchard reagent was similar to that of Δ^7-stenols.[7] The behavior of the acetate of the new sterol (II), m.p. 93–94°, to hydrogenation in glacial acetic acid over Adams catalyst (no hydrogen uptake) was also characteristic of Δ^7- and $\Delta^{8(9)}$-stenols,[8] and resulted in isomerization. The reaction product, m.p. 76–77°, absorbed one mole of hydrogen upon forced hydrogenation in the presence of HCl at 60°[9] to yield a saturated sterol acetate, m.p. 99–101°. The alcohol, m.p. 153–155°, resulting from the hydrolysis of the acetate failed to respond to the Liebermann–Burchard reagent, and its infrared spectrum indicated the absence of double bonds. On Kuhn-Roth C-methyl determination,[10] II liberated 3.48 ± 0.27 equivalents of acetic acid (calcd. as 4-methyl-Δ^7-cholestenyl acetate) or 3.60 ± 0.26 (calcd. as 4,4-dimethyl-Δ^7-cholestenyl acetate). Synthetic 4,4-dimethylcholesteryl acetate,[11] cholesteryl acetate and Δ^7-cholestenyl acetate gave 3.60 ± 0.31, 2.90 ± 0.03, and 3.00 ± 0.22 equivalents of acetic acid, respectively. Thus II possesses approximately one more C-methyl group than the C_{27} sterol acetates (C-methyl = *ca.* 0.6 mole of acetic acid). From chemical and biogenetic considerations, either 4(α or β)-methyl-Δ^7-cholesten-3β-ol or 4,4-dimethyl-Δ^7-cholesten-3β-ol became attractive plausible structures for I. Δ^7-Cholesten-3β-ol was subjected to Oppenauer oxidation to give Δ^7-cholesten-3-one, m.p. 143–145°. This ketone upon treatment with potassium, *t*-butyl alcohol, and methyl iodide, gave a mixture which was reduced with $LiAlH_4$. Purification of the resulting alcohols through the digitonides[12] followed by silicic acid chromatography of the β-sterols afforded two main compounds of m.p. 122–124° and m.p. 146–147°, respectively. The former compound was identical to Δ^7-cholesten-3β-ol, and the latter sterol (less polar) was identical to I (*Anal.* Calcd. for $C_{28}H_{48}O$: C, 84.00; H, 12.00. Found: C, 83.22; H, 12.01) by m.m.p. and infrared spectrum. Evidence has been obtained which tentatively rules out 4,4-dimethyl-Δ^7-cholesten-3β-ol. Future publication of the data will be made. The possibility of the 2(α or β)-methyl isomers cannot as yet be eliminated, but is unlikely on biological grounds. Others[13,14] have reported the monoalkylation of Δ^4-3-one steroids at position 4 using conditions similar to ours. Since these conditions favor the more stable equatorial configuration, it appears likely that I is 4α-methyl-Δ^7-cholesten-3β-ol. The origin of I suggests the possibility that this sterol arises from the

(1) This work was supported by a research grant (H-2458 C, CS) from the National Institutes of Health, U. S. Public Health Services.

(2) Some of the properties of this sterol were studied in collaboration with D. L. Coleman and C. A. Baumann, Department of Biochemistry, University of Wisconsin.

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intestinal mucosa,[3] and that it may be an intermediate in the biosynthesis of cholesterol. Evidence for the existence of demethylated intermediates in the conversion of lanosterol to cholesterol have been reported.[15]

Acknowledgment.—We are indebted to Dr. Hans Noll for infrared measurements, and to Drs. Klaus Hofmann and Arvid Ek for helpful suggestions.

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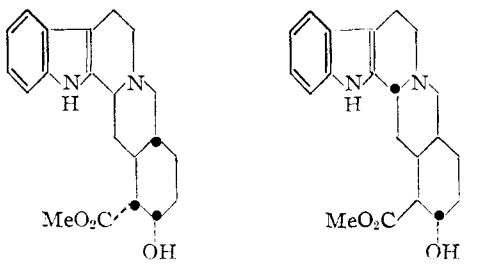
THE STEREOCHEMICAL INTERRELATIONSHIP OF THE YOHIMBINE-TYPE ALKALOIDS[1]

Sir:

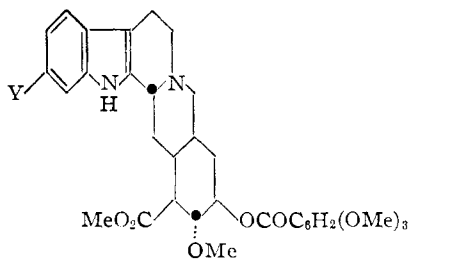
We wish to report the completion of the first phase of our continuing studies of the stereointerrelationship of indole alkaloids containing the ring system of yohimbine, ajmalicine and corynantheine, *i.e.*, the steric relationship of all yohimbine-type alkaloids.

Corynanthine, β-yohimbine and pseudoyohimbine have all been related to yohimbine,[2] whose absolute configuration (I) was ascertained by molecular rotation difference[3] and optical rotatory dispersion[4] studies. Similarly, alloyohimbine, rauwolscine, deserpidine, raunescine and isoraunescine have been interrelated with 3-epi-α-yohimbine[2,5,6]



I

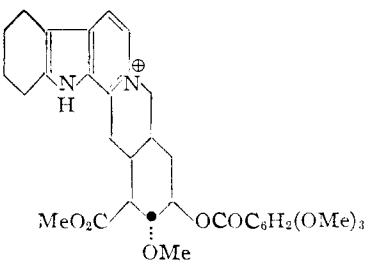
II



III

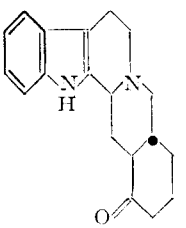
(II). Finally, rescinnamine and pseudoreserpine have been correlated with reserpine[2,6,7] (III, Y = OMe). However, no data chemically relating the three groups of compounds have been reported yet.

Palladium–maleic acid dehydrogenation[8] of reserpine (III, Y = OMe) yielded its tetradehydro derivative (47%) as perchlorate, m.p. 194–196° (Found for $C_{33}H_{37}O_{13}N_2Cl\cdot CH_3OH$: C, 55.11; H, 6.02; N, 3.80). Hydrogenation of the latter with platinum in acetic acid[9] gave the demethoxytetrahydrotetradehydro compound IV (61%), m.p. 188–189°, λ_{max} 250 mμ (log ε 4.16), 270 mμ (log ε 4.10) and 335 mμ (log ε 3.61), $[\alpha]_D$ −40° (chloroform) (Found for $C_{32}H_{35}O_{12}N_2Cl$: C, 55.94; H, 5.25; N, 4.25). The identical product, checked by m.p., mixed m.p., infrared and ultraviolet spectra, and specific rotation, was obtained by the catalytic hydrogenation of the tetradehydro derivative of deserpidine (III, Y = H).[8b] These results constitute the first chemical correlation of compounds of group II and III, and represent a potentially useful method of interrelating the many ring A oxygenated ajmalicine-type alkaloids with alstonine and serpentine.[2]

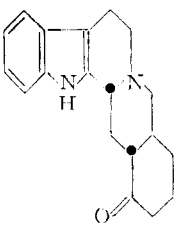


IV

When apoyohimbic acid hydrochloride, readily derivable from yohimbine[2] (I), was exposed to a Schmidt reaction, 16-yohimbone (V), m.p. 256° (dec.), $[\alpha]_D$ −86.1° (pyridine) (Found for $C_{19}H_{22}ON_2$: C, 77.7; H, 7.28; N, 9.3) was obtained in 17% yield.[10] The same reaction, carried out on the *apo* derivative of 3-epi-α-yohimbine[5a] (II), led to a ketone (17%) whose m.p. 254–256°, $[\alpha]_D$ +85.0° (pyridine), and infrared spectrum, identical with that of V, proved it to be the enantiomer of 16-yo-



V



VI

(1) This work was supported in part by a research grant from Ciba Pharmaceutical Products, Inc., and from the National Institutes of Health, Public Health Service, Department of Health, Education and Welfare (M1301).

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