Tetrahedron Letters No.15, pp. 1189-1191, 1969. Pergamon Press. Printed in Great Britain.

THE SYNTHESIS OF SAMANE (DESOXYSAMANINE) AND 17β-HYDROXYSAMANE

Kitaro Oka and Shoji Hara

Division of Organic Chemistry, Tokyo College of Pharmacy

10-19, Ueno-sakuragi 1-chome, Taito-ku, Tokyo 110, Japan

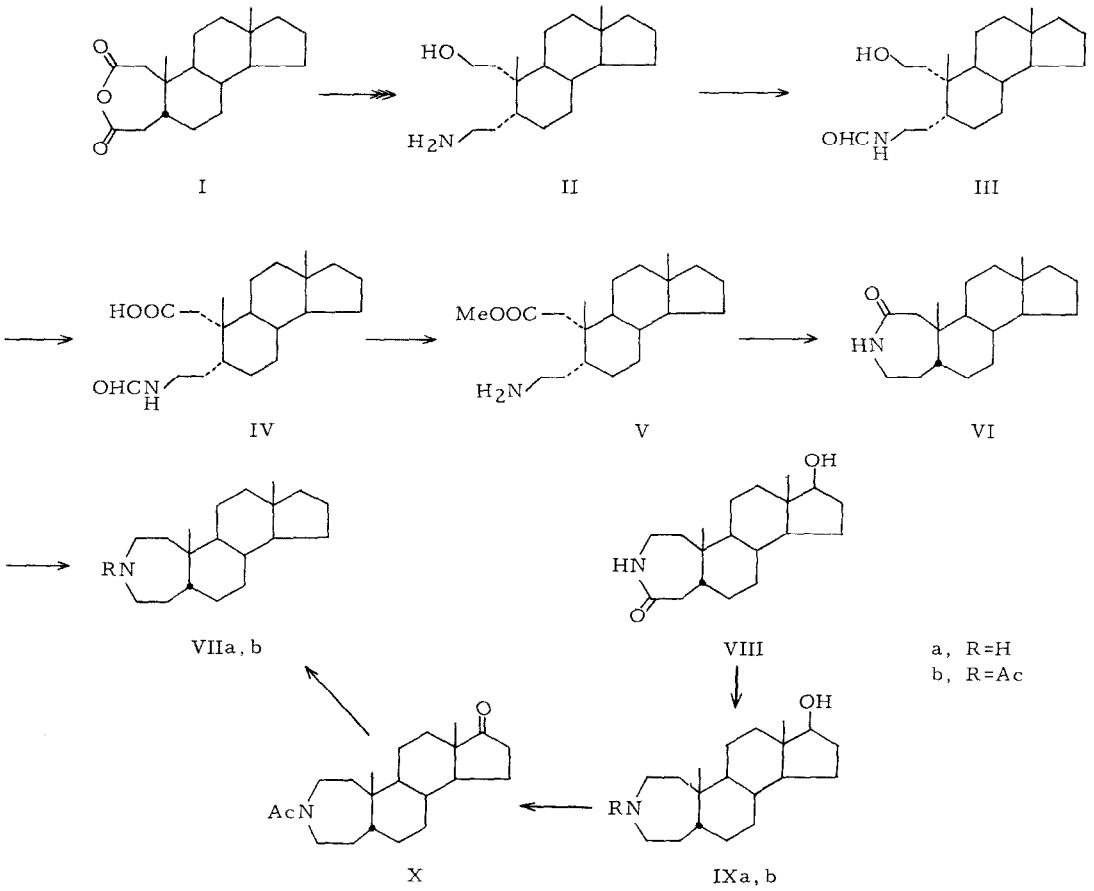
(Received in Japan 7 February 1969; received in UK for publication 24 February 1969)

We have recently reported the quantitative resolution of the geometrical isomers of 17β-hydroxy-5β-androstan-3-one oxime by means of liquid phase column chromatography (1), and their stereospecific Beckmann rearrangement which permitted to give pure 3-aza- and 4-aza-lactams (2). The assignment of pure isomeric forms of oximes and lactams was made by nmr spectrometry (1, 2). In parallel, a secure synthetic sequence for 3-aza-steroid has also been carried out. The present study was undertaken to give chemical support to the structure of the above products obtained in the Beckmann rearrangement, and in connection with this, to synthesize samane (VIIa), one of degradation products of samandarine (3), and possible intermediates (IXa,b) for synthesis of samanine (4) with the same skeleton and a hydroxyl group at 16β-position.

As already reported by us (5, 6), the acid anhydride (I) gave after the three steps sequence the single amino alcohol the structure of which was preliminarily assigned as (II). Formylation of the compound (II) followed by a partial hydrolysis with potassium carbonate gave an amino alcohol (III), $\nu_{max}^{CHCl_3}$: 3300, 1653 cm^{-1}. The alcohol (III) was oxidized with Jones reagent to afford an amidoic acid (IV), mp 176-178°; ν_{max}^{KBr}: 3310, 3000-2300, 1710, 1660 cm^{-1}. Treatment of the carboxylic acid (IV) with dry hydrogen chloride in absolute methanol resulted in methylation of the acid group and cleavage of the amide group to yield an amino ester (V), mp of hydrochloride 203-205°; ν_{max}^{KBr}: 1729 cm^{-1} Cyclization of the amino ester (V) into a 3-aza-lactam was accomplished by heating (V) in n-butanol under reflux. Its nmr spectrum revealed an AB quartet, almost triplet, centered at δ 2.42 ppm (J=15 Hz) corresponding to

$COCH_2$ protons and an unresolved multiplet corresponding to NCH_2 protons at δ 3.20 ppm so that the structure could be depicted as 2-oxo-3-aza-lactam (VI), mp 200-201°.

Reduction of the lactam (VI) with lithium aluminum hydride in tetrahydrofuran gave a secondry amine (VIIa) which was acetylated with acetic anhydride in pyridine to give an acetamide (VIIb),* mp 55-60°; $\nu_{max}^{CHCl_3}$: 1628 cm^{-1}; $\delta_{TMS}^{CDCl_3}$: 0.70 (singlet, 13β-CH_3), 1.00 (singlet, 10β-CH_3), 2.08 ppm (multiplet, $N(CH_2)_2$).



* The compounds (VIIa) and (VIIb) have been synthesized by Shoppee et al. (7) by the methods involving the Beckmann rearrangement of the oxime mixture of 5β-androstan-3-one and separation of the mixture of resultant lactams by repeated recrystallization. They observed the melting points of 52-56° and 74-76° for (VIIa) and (VIIb), respectively.

A series of reactions was carried out as mentioned bellow with the lactam (VIII) obtained by the Beckmann rearrangement in our previous paper (2). The lactam (VIII) was reduced with lithium aluminum hydride to afford an amino alcohol (IXa), mp 220-223°; ν_{max}^{KBr}: 3260 (NH overlapped with OH), which is an isomer of samanine with respect to the hydroxy position. Protection of the amino group of (IXa) as an acetamide (IXb), mp 186-188°, was achieved by acetylation and subsequent partial hydrolysis with an equimolar amount of potassium hydroxide. The hydroxyl group of (IXb) was oxidized with Jones reagent to give a ketone (X), $\nu_{max}^{CHCl_3}$: 1740, 1629 cm^{-1}, which was reduced by the Huang-Minlon modification of the Wolff-Kishner reduction and then acetylated to give the acetamide (VIIb).

Identification of both (VIIb) prepared by the separate routes mentioned above was successful in all respects, ir and nmr spectra, tlc and gas chromatography, and mixed melting point test. From the physical data obtained here the amine (VIIa) was recognized to be identical with samane, and also have the same structure as that of erroneously proposed neosamane which was revised later to the 10α-methyl epimer (8).

We wish to thank Miss K. Shinjo for her technical assistance. The financial support from the Ministry of Education in Japan as a Grant-in-Aid for Scientific Research is acknowledged.

REFERENCES

1. K.Oka and S.Hara, Chem. Ind., 911 (1968).
2. K.Oka and S.Hara, ibid., in press.
3. C.Schöpf and O.W.Müller, Ann. Chem., 633, 127 (1960).
4. G.Habermehl, The Alkaloids, Vol.IX, p.427. Academic Press, New York (1967).
5. S.Hara and N.Matsumoto, Yakugaku Zasshi, 85, 48 (1965).
6. S.Hara and M.Miyaki, Ann. Rep. Tokyo Coll. Pharm., 16, 10 (1966).
7. C.W.Shoppee and G.Krueger, J. Chem. Soc., 3641 (1961).
8. G.Habermehl and S.Göttlicher, Chem. Ber., 98, 1 (1965).