4,17a-Diaza-D-homoandrostane Lactams,[1] a New Hetero-steroid System

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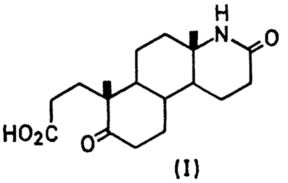
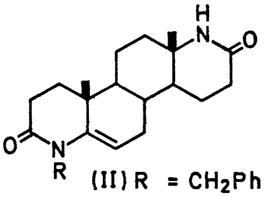
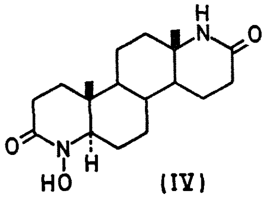
Summary Compounds related to a new 4,17a-diaza-D-homosteroid system have been prepared by reactions with 17a-aza-5,17-dioxo-D-homo-3,5-seco-4-norandrostan-3-oic acid.

IN continuation of our work on the synthesis of new hetero-steroid systems the analogues of which may be of medicinal significance, we report a new diaza-D-homo-skeleton achieved through the preparation of 4,17a-diaza-D-homo-androstane lactams.

17a-Aza-D-homoandrost-4-en-3-one,[2] on oxidation with the periodate–permanganate reagent of Lemieux and von Rudloff[3,4] gave the seco-keto-acid (I), m.p. 266—267° (77% yield), $C_{18}H_{27}NO_4$, ν_{max} (KBr) 3320, 2970, 2930, 2860, 1700, and 1610 cm^{-1}. The compound (I) was also characterized by preparation of its oxime by heating with hydroxylamine hydrochloride and pyridine; m.p. 247—248° (84% yield), ν_{max} (KBr) 3270 (broad), 1680, and 1610 cm^{-1}.


(I)


(II) R = CH_2Ph
(III) R = $CH_2{\cdot}CH_2OH$


(IV)

The seco-keto-acid (I), on heating under reflux with benzylamine, afforded a compound, m.p. 278—280° (62% yield), $[\alpha]_D^{20}$ −127·2° (*c* 1·05, $CHCl_3$), analysing for $C_{25}H_{32}N_2O_2$, which was assigned the structure 4-benzyl-4,17a-diaza-D-homoandrost-5-ene-3,17-dione (II) on the basis of the spectral data, λ_{max} (MeOH) 234 nm (ϵ 10,110) indicative of an enamine system, ν_{max} (KBr) 1655 and 1625 cm^{-1}. Similarly, the dilactam (III) was prepared by treatment of (I) with ethanolamine, m.p. 238—240° (21% yield), $[\alpha]_D^{20}$ −109·3° (*c* 1·16, $CHCl_3$), λ_{max} (MeOH) 235 nm (ϵ 10,200), ν_{max} (KBr) 3335 and 1645 cm^{-1}, and showing satisfactory elemental composition.

Reduction of the oxime of (I) with zinc and acetic acid gave the hydroxamic acid (IV), m.p. >300° (70% yield), ν_{max} (KBr) 3310, 3230, 3175, and 1640 (broad) cm^{-1}, giving with methanolic ferric chloride an immediate pink-violet colour, turning to green. The structure (IV) was assigned by analogy with products of similar reductions.[5]

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[3] R. U. Lemieux and E. von Rudloff, *Canad. J. Chem.*, 1955, 33, 1701 and 1710.
[4] E. von Rudloff, *Canad. J. Chem.*, 1955, 33, 1714; 1956, 34, 1413.
[5] J. T. Edward and P. F. Morand, *Canad. J. Chem.*, 1960, 38, 1316.