547. *Steroid Hormones. Part XIII.*[1] *13-Aza- and 13-Aza-*D-*homo-analogues of Equilenin Methyl Ether*

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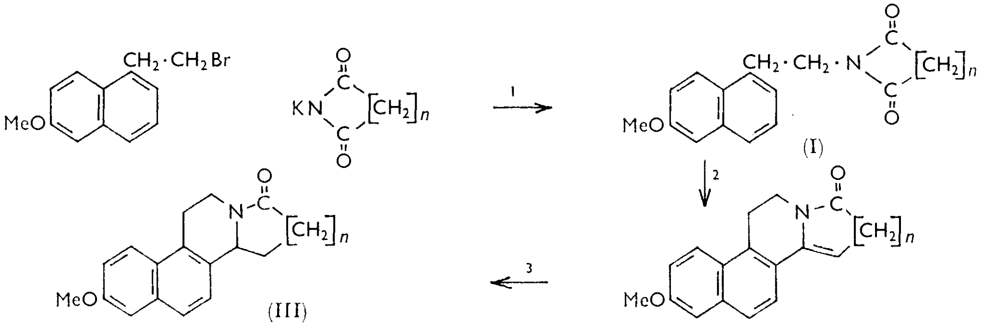
Some aza-analogues of steroid hormones have been made with a nitrogen atom in, for example, the 4-,[2] the 6-,[3] and the 8-position.[4] The presence of such a nitrogen has not led so far to any compound of hormonal interest. The presence of a non-basic nitrogen, in an amide group, in a hormone analogue seemed more likely to lead to interesting compounds, and we report the first preparation of the (±)-13-aza-(III; $n = 1$) and (±)-13-aza-D-homo-analogue (III; $n = 2$) of equilenin methyl ether.



Reagents: 1, Dimethyl sulphoxide; 2, polyphosphoric acid; 3, H_2–Pd

These were readily synthesised, from the potassium salts of succinimide or glutarimide, provided that dimethyl sulphoxide was used as the solvent for the initial condensation. No other solvent gave the desired product. The methods tried included reaction in liquid ammonia, and of the potassium salts in refluxing xylene with the bromide. Dimethylformamide gave a crude product which, from infrared spectra, seemed to contain some of the desired product, but this could not be isolated.

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Experimental.—N-[2-(6-*methoxy*-1-*naphthyl*)*ethyl*]*glutarimide* (I; *n* = 3). Glutarimide (6 g.) in ethanol (15 c.c.) containing dissolved potassium (2 g.) was briefly refluxed, and the solution evaporated to dryness under reduced pressure. A mixture of 2-(6-methoxy-1-naphthyl)ethyl bromide [5] (1 g.) and potassium glutarimide (3 g.) in dimethyl sulphoxide (20 c.c.) was shaken for 8 hr., poured into water (50 c.c.), and extracted with ether. The *product* (0·91 g.) formed needles, m. p. 120—121° (from methanol) (Found: C, 72·7; H, 6·4; N, 4·65. $C_{18}H_{19}NO_3$ requires C, 72·7; H, 6·4; N, 4·7%), $\lambda_{max.}$ 230, 265, 275, 287 mμ (ε 34,260, 7130, 8120, 6730), $\nu_{max.}$ 1712, 1662, 1640, 1600, 1518 cm.$^{-1}$.

(±)-13-*Aza*-14(15)-*dehydro*-D-*homo*-18-*norequilenin methyl ether* (II; *n* = 2). The above glutarimide (0·7 g.) was heated for 3 min. at 145° with a solution of phosphorus pentoxide (2·5 g.) in phosphoric acid (3 c.c.; *d* 1·75). Water was added, the mixture was extracted with ether, washed with sodium hydroxide solution (2%), and dried. The *product* (0·42 g.), crystallised twice from ethanol, had m. p. 182—183° (Found: C, 77·25; H, 6·4; N, 5·3. $C_{18}H_{17}NO_2$ requires C, 77·4; H, 6·1; N, 5·0%), $\lambda_{max.}$ 245, 254, 305 mμ (ε 17,910, 20,420, 3288), $\nu_{max.}$ 1660, 1620, 1600, 1520 cm.$^{-1}$; p.m.r. spectrum: multiplet at 2·10, 2·28, and 2·42 (5H) (naphthalene protons); resonances at 6·13 (OMe), 6·90 (4H), and 7·50 (4H) (alicyclic methylenes, and at 4·2 (remaining olefinic proton).

(±)-13-*Aza*-D-*homo*-18-*norequilenin methyl ether* (III; *n* = 2). 13-Azadehydro-D-homo-equilenin methyl ether (0·5 g.) in ethanol (50 c.c.) was hydrogenated in the presence of palladium–charcoal (200 mg.; 10%); 1 mole of hydrogen was absorbed in 1 hr. The *product* (0·38 g.) had m. p. 174—175° (from acetone) (Found: C, 77·0; H, 6·55; N, 5·1. $C_{18}H_{19}NO_2$ requires C, 76·85; H, 6·8; N, 5·0%), $\lambda_{max.}$ 236, 264, 274, 285 mμ (ε 49,960, 9400, 9360, 6245), $\nu_{max.}$ 1630, 1600, 1580, 1510 cm.$^{-1}$.

(±)-13-*Aza*-18-*norequilenin methyl ether* (III; *n* = 1). Reactions were carried out as above, but with a molar equivalent of potassium succinimide. The N-[2-(6-*methoxy*-1-*naphthyl*)*ethyl*]-*succinimide* had m. p. 135—136° (from ethanol) (Found: C, 72·6; H, 5·65; N, 4·5. $C_{17}H_{17}NO_3$ requires C, 72·1; H, 6·05; N, 4·9%), $\lambda_{max.}$ 262, 271, 284 mμ (ε 10,190, 12,290, 9835), $\nu_{max.}$ 1695, 1620, 1600, 1520 cm.$^{-1}$. The 13-aza-14(15)-dehydro-18-norequilenin methyl ether obtained by cyclisation did not crystallise, but the gum had the expected spectra: $\lambda_{max.}$ 245, 250, 312 mμ (ε 18,600, 21,020, 3800), $\nu_{max.}$ 1688, 1618, 1600, 1518 cm.$^{-1}$. After hydrogenation, the (±)-13-*aza*-18-*norequilenin methyl ether* had m. p. 168—170° (from acetone) (Found: C, 76·9; H, 6·2; N, 5·2. $C_{17}H_{17}NO_2$ requires C, 76·4; H, 6·4; N, 5·2%), $\lambda_{max.}$ 265, 275, 285 mμ (ε 10,200, 10,120, 9600), $\nu_{max.}$ 1692, 1625, 1600, 1520 cm.$^{-1}$.

We are indebted to Syntex S.A. for financial assistance.

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[*Received, October* 23*rd*, 1964.]

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