CCLXXVIII. NOTE ON TWO DERIVATIVES OF OESTRONE

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IN connexion with some other investigations we had occasion to prepare *oestrone β -naphthoate* and *oestrone diethylaminoethyl ether*. Neither of these substances appears to have been previously described and we have had them tested for oestrogenic activity. *Oestrone α -naphthoate* has been prepared by MacCorquodale *et al.* [1936], but no record was made of its oestrogenic activity. *Oestrone β -naphthoate* resembles the corresponding benzoate [Butenandt, 1930] in that it produces in rats a prolonged period of oestrus although the onset of oestrus is delayed longer than with *oestrone* itself. The diethylaminoethyl ether of *oestrone* is of interest as it yields water-soluble salts, but when tested in rats it showed little or no oestrogenic activity.

EXPERIMENTAL

Oestrone β -naphthoate. A solution of *oestrone* (0.5 g.) and β -naphthoyl chloride (0.6 g.) in pyridine (2.5 ml.) was kept at room temperature for 12 hr. and then heated to 70° for 1 hr. On pouring into a mixture of crushed ice and H_2SO_4 a white solid separated which was collected, washed with aqueous Na_2CO_3 , then with water and dried. Extraction with amyl ether gave a small amount of β -naphthoic anhydride and the residue was practically insoluble in diethyl ether. The crude product (0.6 g.) was insoluble in water and glacial acetic acid and very sparingly soluble in alcohol, ethyl acetate and ligroin. Recrystallized from dioxane it had m.p. 262–264°. (Found: C, 81.8; H, 6.4%. $\text{C}_{29}\text{H}_{28}\text{O}_3$ requires C, 82.1; H, 6.6%.)

Biological test. In rats doses of 600 and 100 γ produced oestrus after 100 hr. lasting for 10 days; 24, 12, 6 γ produced oestrus after 100 hr. lasting for 4 days. The threshold dose appeared to be between 1 and 2.5 γ .

Oestrone diethylaminoethyl ether. A mixture of *oestrone* (50 mg.) diethylaminoethyl chloride (120 mg.) and aqueous KOH (25 ml. of 30%) was heated on the water bath for 2 hr., during which time the *oestrone* slowly dissolved. After cooling and diluting with water the mixture was filtered. The filtrate acidified with HCl gave a precipitate of *oestrone* (11 mg.) which was collected, and the mother liquor combined with the solution obtained by dissolving the initial filter residue in dilute HCl. The combined acid solutions were again made alkaline and the solid precipitate collected and recrystallized from dilute alcohol. The diethylaminoethyl ether of *oestrone* (42 mg.) formed glittering leaflets. m.p. 76–77°. (Found: N, 4.0%. $\text{C}_{24}\text{H}_{37}\text{O}_2\text{N}$ requires N, 3.8%.) In biological tests it showed no oestrogenic activity in doses of 6, 100 and 1000 γ . The base dissolved

in alcohol and treated with ethereal HCl gave the *hydrochloride*, which, crystallized from a mixture of absolute alcohol and ethyl acetate, had m.p. 190–191°.

The biological tests were carried out by Messrs Hoffman-La Roche and Co., Basle, to whom we express our thanks.

REFERENCES

- Butenandt (1930). *Hoppe-Seyl. Z.* **191**, 140.
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