*A Nitrogen Analog of Hexestrol, Ethyl-p-hydroxyphenyl-(1-p hydroxyphenyl-propyl)-amine, and Its Derivatives**

By Yujiro NOMURA

(Received January 11, 1954)

Various oxygen and sulfur analogs of hexestrol have been prepared and found to have estrogenic activities [1] These facts show that the member constituting the molecular skeleton of hexestrol may be replaced by a different atom without destroying totally the estrogenic activity, unless a significant change in the molecular shape and the appearance of any new physiological properties are associated with the introduction of the different atom.

The author prepared a nitrogen analog of hexestrol, ethyl-*p*-hydroxyphenyl-(1-*p*-hydroxyphenyl-propyl)-amine, *p*-$HOC_6H_4N(C_2H_5)CH(C_2H_5)C_6H_4OH$-*p*, as follows Dry hydrogen bromide was passed into an ethereal solution of anethole (3 11 g), and the resulting solution of the addition product was mixed with a pyridine solution containing an equivalent amount of ethyl-*p*-methoxyphenyl-amine, prepared according to King and Tonkin [2] After standing overnight the reaction mixture was shaken with water. From the upper layer ethyl-*p*-methoxyphenyl - (1-*p* - methoxyphenyl-propyl)-amine (3.39 g) was isolated and recrystallization from methanol gave colorless prisms, melting at 64 5–65 0°C Found C, 76 20 , H, 8.50; N, 4 70 Calculated for $C_{19}H_{25}O_2N$. C, 76 22 , H, 8 42 , N, 4 68%.

This amine developed incomplete but distinct durable estrus in the dosage of 60 *γ* by subcutaneous injection into ovariectomized mice in two portions in oil solution as referred to elsewhere.[3]

Ethyl-*p*-hydroxyphenyl-(1-*p*-hydroxyphenyl-propyl)-amine was obtained by the demethylation of the above substance with red phosphorus and hydroiodic acid (d=1.7) in colorless crystals melting at 100 5°C. after recrystallization from benzene Found: C, 75 32 , H, 7 61; N, 5 30. Calculated for $C_{17}H_{21}O_2N$ · C, 75 24 , H, 7 80; N, 5 16%.

Acetylation of ethyl-*p*-hydroxyphenyl-(1-*p*-hydroxyphenyl-propyl)-amine with acetic anhydride gave a diacetate melting at 54–55°C. Found N, 3 61. Calculated for $C_{21}H_{25}O_4N$: N, 3 94%.

The author wishes to express his hearty thanks to Professor Y. Urushibara for his kind guidance and encouragement. Thanks are also due to Mr. F. Ueno, Teikoku Hormone Manufacturing Co., Ltd., Kawasaki, for the bio-assays and to the Ministry of Education for the Grant in Aid for Fundamental Scientific Research

Chemical Institute, College of General Education
Tokyo University, Tokyo

* All melting points are corrected

1) Y Urushibara and M Ōki, This Bulletin, **23**, 35 (1950) Y Urushibara and T Takahashi, ibid, **23**, 53 (1950), Y Urushibara and M. Ōki and R Ikeda, ibid, 25, 66 (1952)

2) Harold King and Isabel M Tonkin, *J. Chem Soc*, **1946**, 1063

3) Y. Urushibara and T. Takahashi, This Bulletin, **23**, 54 (1950).