

PREPARATION OF

17-KETO(OR HYDROXY)-5'-ALKYL(OR ARYL)-ESTRA-1(10),4-DIENO [3,2-b] FURANS

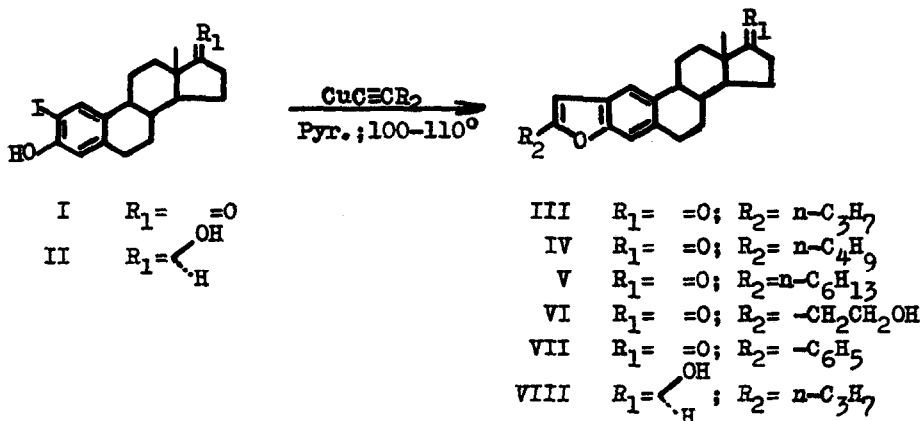
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An increasing interest in the chemistry of heterocyclic steroids having a hetero-ring fused to the ring A of steroid nucleus (1), has provoked us to present a simple 2-step method for the synthesis of title compounds. The literature reports on the heterocyclic steroids containing furan ring attached to the ring A of steroid nucleus have been insofar sparse (2,3). Moreover, all the published methods can be hardly used as a straightforward route for the preparation of these compounds.

We prepared the title steroids from estrone and estradiol in two steps: (1) iodination in presence of Hg^{2+} according to the known procedure (4) afforded the corresponding 2-iodo derivatives (I and II); and (2) these were reacted with different cuprous acetylides in boiling pyridine (5) yielding directly the new furan steroids[¶]:



¶ 2-Alkynyl-estrone or estradiols, which are obviously intermediates in this substitution reaction (5), could not be isolated because spontaneous cyclization into III-VIII took place.

The new furans III-VIII, after chromatographic purification on a silica gel column (benzene-ethyl acetate 97:3), were obtained as white crystalline compounds in ca. 70% yields (based on starting estrone and estradiol). Their structures were easily confirmed taking into account both spectral and chemical evidence. Thus, for example, III ($R_1 = \text{=O}$; $R_2 = n\text{-C}_3\text{H}_7$) has the following characteristics: m.p. 124-125°C. (acetone); $[\alpha]_D^{24}$: +180° (c=1.0, CHCl_3); found: C, 82.00; H, 8.43; calcd. for $\text{C}_{23}\text{H}_{28}\text{O}_2$: C, 82.10; H, 8.39; IR spectrum (KBr): 1744 (carbonyl), 1212, 1144 (C-O), and 885 cm^{-1} (1,2,4,5-tetrasubstituted benzene); NMR spectrum ($\text{CCl}_4 + \text{TMS}$): singlet at 6.416 δ (4'H), doublet at 7.265 δ (aromatic protons of benzene ring); Mass spectrum: maxima at 336 (molecular ion M^+) and 307 mass units ($\text{M}^+ - \text{C}_2\text{H}_5$). Similar data were obtained for IV-VIII.

The new compounds, III-VIII, exhibit all the properties typical for furan derivatives. Thus, with peracids or O_3 the furan ring can be opened giving rise to 2-carboxy-estrone esters. These esters, after hydrolysis of the acyloxy group and subsequent reduction of the 2-carboxy group, afford 2-hydroxymethylestrone. However, these and related reactions will be the subject of forthcoming communication.

REFERENCES

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