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AN AROMATIC C-RING ANALOG OF 18-NORESTRONE

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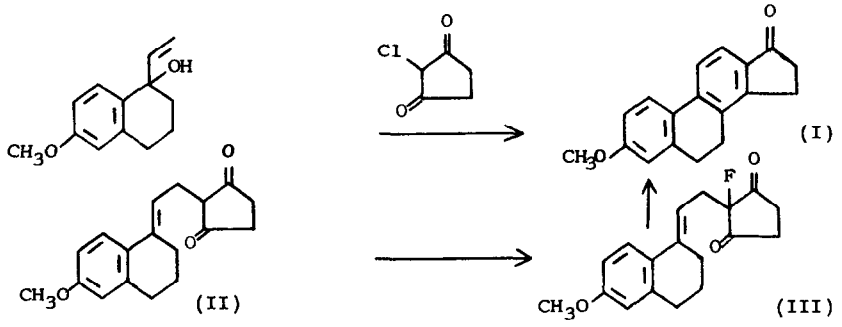
We have prepared a steroid hormone analog having aromatic A and C-rings, which has no asymmetric carbon atoms in the molecule (1).

Condensation of 1,2,3,4-tetrahydro-6-methoxy-1-vinyl-1-naphthol (2) with 2-chlorocyclopentane-1,3-dione (3) in refluxing xylene, containing t-butanol and a catalytic amount of Triton B, afforded as the main product, a ketone: m.p. 141-142°C; (4) I.R. 5.9μ; (5) U.V. $\lambda_{max.}^{MeOH}$ 328 (ε, 27.700). In addition to the A-ring resonances, its NMR spectrum (in $CDCl_3$, TMS as internal standard) showed a 2 proton singlet at 2.32 τ attributed to the aromatic protons at C-11 and C-12, a 4 proton singlet at 7.14 τ attributed to the protons at C-6 and C-7, as well as a pair of multiplets (2 protons each) centered at 6.95 and 7.25 τ, (5) for the protons at carbons 15 and 16 respectively. On the basis of these spectral data, the compound was assigned the 3-methoxy-17-keto-gona-1,3,5(10),8,11,13(14)-hexa-ene structure (I).

An alternate synthesis involved the treatment of 2-[2-(3,4-dihydro-6-methoxy-1(2H)-naphthylidene)ethyl]-cyclopentane-1,3-dione (II) (6) with ClO_3F in pyridine, affording the corresponding tricyclic fluorodione (III): m.p. 104-105°C; I.R. 5.59 and 570μ; U.V. $\lambda_{max.}^{MeOH}$ 260, (ε, 18.600), which upon cyclization in acetic acid with p-toluenesulfonic acid, yielded the same ketone (I).



References

1. (a) Aromatic C-ring steroids have been reported in the modified ergosterol series, in which ring C aromatization was accompanied by migration of the angular methyl group from C-13 to C-12. C. F. Hammer, D. S. Savage, J. B. Thomson and R. Stevenson, Tetrahedron 20, 929 (1964); D. Levy and R. Stevenson, Tetrahedron Letters, 1966, 3063. (b) A very recent communication by A. J. Birch and G. S. R. Subba Rao, Tetrahedron Letters, 1967, 857; described a C-aromatic bisnorsteroid having a phenolic hydroxyl at C-11.

2. (a) I. N. Nazarov, I. V. Torgov and G. P. Verkholetova. Dokl. Akad. Nauk SSSR, 112, 1067 (1957); (b) see C. H. Kuo, D. Taub and N. L. Wendler. Angew. Chem., Intern. Ed. Eng. 4, 1083 (1965) for mechanistic considerations.

3. J. R. Beckwith and L. P. Hager, J. Biol. Chem. 238, 3091 (1963). Preferably obtained by chlorinating cyclopentane-1,3-dione witn N-chlorosuccinimide in acetic acid.

4. All new compounds have satisfactory elemental analyses.

5. A recent paper by M. M. Coombs, J. Chem. Soc. (C), 1966, 955; describes 15,16-dihydro-17-oxocyclopenta[a]phenanthrene; I.R. 5.92μ; NMR: multiplets for CH_2 protons on C-15 at 6.72, and on C-16 at 7.3τ.

6. Prepared by Dr. J. Hannah and K. W. Kelly of these laboratories.