# Steroidal Imidazo-Pyridines

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In connection with our studies of the physiological activity of modified nitrogen steroids (2), it was found of interest to effect the reaction of 2-aminomethylpyridine with steroidal bromoketones.

2-Aminopyridine generally reacts with an alkyl halide to produce substitution on the ring nitrogen, while sodium 2-aminopyridine leads only to amino group substitution (3,4).

Chichibabin (5) has shown that the reaction of α-halo ketones with 2-aminopyridine gives imidazo[1,2-*a*]pyridine.

Extension of this reaction to 3β-acetoxy-16α-bromo-5α-androstan-17-one (6) and 3β-acetoxy-16α-bromo-5-androsten-17-one (7) with 2-aminomethylpyridine in xylene forms the corresponding imidazopyridines.

The structure assignment of III is supported by ir and nmr.

Condensation of 2-amino-4-methylpyridine and 21-bromo-3β-hydroxy-5-pregnen-20-one (9) gives the corresponding imidazopyridine (V) in 43% yield.

The structure assignment of V is supported by ir absorption at 3300 (OH), 1640 (C=N) $cm^{-1}$ and nmr at $\tau$ 1.35 ($C_3'$-H), 2.25 ($C_5'$-H), 2.5 ($C_8'$-H), 2.9 ($C_6'$-H) and 7.6 ($C_7'$-$CH_3$).

## EXPERIMENTAL

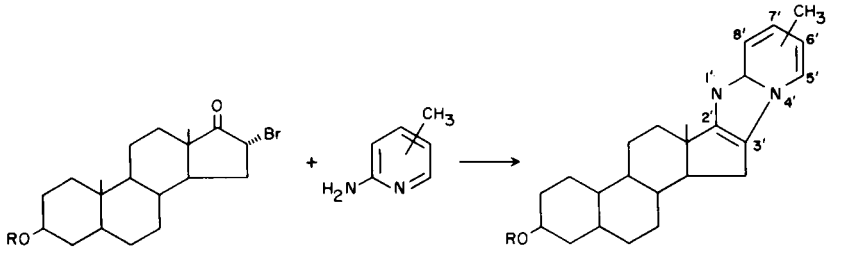
Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Ir spectra were recorded with a Perkin-Elmer 521 in solid phase potassium bromide. Nmr spectra were determined with a Varian Associates A-60 instrument, using deuteriochloroform as a solvent and tetramethylsilane as the internal standard. Elemental analyses were performed by the Analytical Laboratory of the Chemistry Division, Democritos.

General Procedures for the Preparation of Steroidal Methylimidazo[1,2-*a*]pyridines.

To a solution of 5 mmoles of bromoketone in 20 ml. of anhydrous xylene was added 10 mmoles of 2-aminomethylpyridine and the mixture was refluxed for 24-48 hours. After filtration of the reaction mixture, the solvent was evaporated under reduced pressure. The remaining residue was dissolved in chloroform and the solution washed several times with water, dried over sodium sulfate and evaporated under reduced pressure to give a residue which on recrystallization from the appropriate solvent yielded the corresponding methylimidazo[1,2-*a*]pyridines. The compounds prepared are reported in Table I.

3β-Hydroxy-5-pregneno[20,21:2′,3′]methyl-7′-imidazo[1′,2′-*a*]pyridine (V), was prepared as described for III using 21-bromo-3β-hydroxy-5-pregnen-20-one. The product was crystallized from methanol (43%), m.p. 155-157°.

*Anal.* Calcd. for $C_{27}H_{35}N_2O$: C, 80.40; H, 8.91; N, 6.93. Found: C, 80.77; H, 8.63; N, 6.96.

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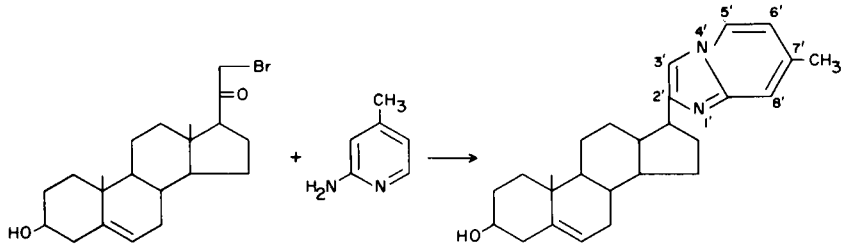


IV V

TABLE I

3β-Acetoxy-5α-androstano[16,17:2′,3′]methylimidazo[1′,2′-*a*]pyridines (III)

| No. | R | $CH_3$ | M.p., °C | Formula | Yield % | Analyses Calcd. % C | H | N | Found % C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| III | $COCH_3$ | 8′ | 214-215 | $C_{27}H_{36}N_2O_2$ | 48 | 77.14 | 8.57 | 6.66 | 76.80 | 8.30 | 6.84 |
| IIIa | $COCH_3$ | 7′ | 269-270 | $C_{27}H_{36}N_2O_2$ | 48 | 77.14 | 8.57 | 6.66 | 76.85 | 8.36 | 6.66 |
| IIIb | $COCH_3$ | 6′ | 256-257 | $C_{27}H_{36}N_2O_2$ | 45 | 77.14 | 8.57 | 6.66 | 76.70 | 8.57 | 6.83 |
| IIIc | $COCH_3\Delta^5$ | 7′ | 243-245 | $C_{27}H_{34}N_2O_2$ | 42 | 77.33 | 8.35 | 6.68 | 76.87 | 7.97 | 6.58 |

Recrystallization Solvents: III, IIIa, IIIb ($CH_3COOC_2H_5$) and IIIc ($CH_3OH$).

TABLE II

Nmr of 3β-Acetoxy-5α-androstano[16,17:2′,3′]methylimidazo[1′,2′-*a*]pyridines (III) (9)

| No. | $C_5'$-H | $C_6'$-H | $C_7'$-H | $C_8'$-H |
|---|---|---|---|---|
| III | 2.20 | 3.3 | 3.1 | 7.35 ($C_8'$-$CH_3$) |
| IIIa | 2.15 | 3.3 | 7.55 ($C_7'$-$CH_3$) | 2.6 |
| IIIb | 2.25 | 7.7 ($C_6'$-$CH_3$) | 3.1 | 2.55 |
| IIIc | 2.25 | 7.65 ($C_6'$-$CH_3$) | 3.0 | 2.50 |

$\nu$ max: 1720, 1240 ($CH_3CO$) and 1640 (C=N) $cm^{-1}$.

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