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SYNTHESIS OF STEROIDAL NITROIMIDAZOLES

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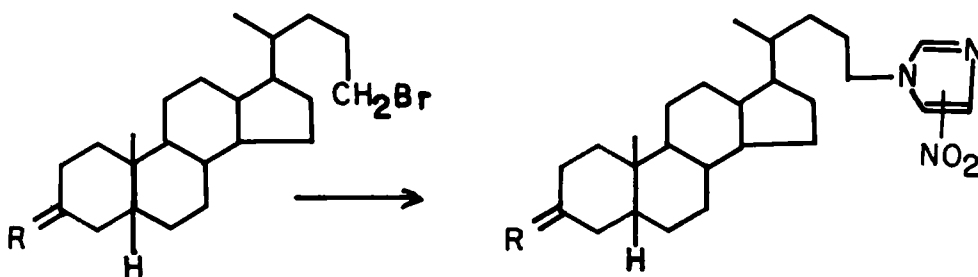
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SYNTHESIS OF STEROIDAL NITROIMIDAZOLES

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(6/9/75)

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Although substituted nitroimidazoles are known to have antibacterial and antiprotozoal activities,¹⁻³ no steroidal nitroimidazoles have, until now, been described in the literature.



Ia, R = H,H
Ib, R = ethylenedioxy

IIa, R = H,H
IIb, R = ethylenedioxy
IIc, R = O

Compounds IIa and IIb were prepared⁴ from the reaction of halides Ia and Ib^{5,6} with the sodium salt of 4-nitroimidazole in N,N-dimethylformamide. This reaction gave a fair yield of a equimolar mixture of 4-nitro and 5-nitroimidazolyl steroid, as shown by nmr spectroscopy. Compound IIc was obtained from IIb by mild acid hydrolysis.

JAMES A. MOORE

EXPERIMENTAL

Microanalyses were carried out by Joseph Alicino, Metuchen, N. J., U.S.A.

24-[4-(5-)-Nitroimidazolyl]-5 β -cholane (IIa). - A mixture of 2.0 g of 24-bromo-5 β -cholane (Ia) and 0.5 g of the sodium salt of 4-nitroimidazole⁷ in 50 ml of N,N-dimethylformamide was heated at reflux for 36 hrs. The solution was filtered and the filtrate was evaporated at reduced pressure. The residue was purified by dry-column chromatography on silica gel with chloroform as the developing agent. White crystals, mp. 197-9 $^{\circ}$, $[\alpha]_D + 55^{\circ}$ (CHCl₃) nmr 7.4(s), 7.8(s) ppm (1.4 g, 65%) were obtained.

Anal. Calcd. for C₂₇H₄₃N₃O₂: C, 73.43; H, 9.81; N, 9.51.
Found: C, 73.64; H, 9.57; N, 9.01.

24-[4-(5-)-Nitroimidazolyl]-3,3-ethylenedioxy-5 β -cholane (IIb). This compound was prepared and purified in a similar way to IIa, mp. 160-1 $^{\circ}$, $[\alpha]_D + 17^{\circ}$ (CHCl₃) nmr δ 7.4, 7.8 (s); yield, 1.2g, 55%.

Anal. Calcd. for C₂₉H₄₅N₃O₄: C, 69.71; H, 9.08, N, 8.41.
Found: C, 69.90; H, 8.91; N, 8.64.

24-[4-(5-)-Nitroimidazolyl]-5 β -cholan-3-one (IIc). - A solution of 1.0 g of IIb in 15 ml of glacial acetic acid was warmed to 90 $^{\circ}$, and 5 ml of distilled water was added slowly with stirring, under nitrogen. After one hour, the reaction mixture was poured into ice-water and the resulting suspension was filtered. Recrystallization from acetone-hexane gave IIc, mp. 185-7 $^{\circ}$, $[\alpha]_D + 77^{\circ}$ (CHCl₃), nmr δ 7.4, 7.7 (s), ir 1735 cm⁻¹,

yield 0.9 g (87%).

Anal. Calcd. for $C_{27}H_{41}N_3O_3$: C, 71.17; H, 9.07; N, 9.22.

Found: C, 71.39; H, 9.10; N, 8.85.

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