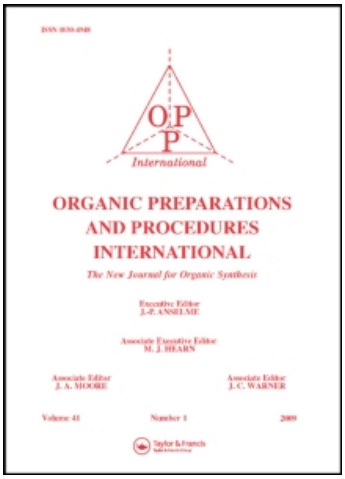

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SYNTHESIS OF STEROIDAL NITROIMIDAZOLES

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SYNTHESIS OF STEROIDAL NITROIMIDAZOLES

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(6/9/75)

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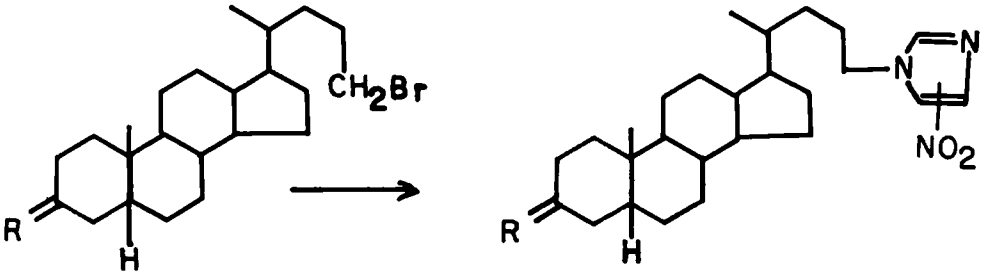
Although substituted nitroimidazoles are known to have antibacterial and antiprotozoal activities,[1-3] no steroidal nitroimidazoles have, until now, been described in the literature.



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

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

Compounds IIa and IIb were prepared[4] 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.

EXPERIMENTAL

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

24-[4-(5-)-Nitroimidazolyl]-5β-cholane (IIa). - A mixture of 2.0 g of 24-bromo-5β-cholane (Ia) and 0.5 g of the sodium salt of 4-nitroimidazole[7] 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°, $[\alpha]_D$ + 55° ($CHCl_3$) nmr 7.4(s), 7.8(s) ppm (1.4 g, 65%) were obtained.

Anal. Calcd. for $C_{27}H_{43}N_3O_2$: 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-5β-cholane (IIb). This compound was prepared and purified in a similar way to IIa, mp. 160-1°, $[\alpha]_D$ + 17° ($CHCl_3$) nmr δ 7.4, 7.8 (s); yield, 1.2g, 55%.

Anal. Calcd. for $C_{29}H_{45}N_3O_4$: C, 69.71; H, 9.08, N, 8.41.
Found: C, 69.90; H, 8.91; N, 8.64.

24-[4-(5-)-Nitroimidazolyl]-5β-cholan-3-one (IIc). - A solution of 1.0 g of IIb in 15 ml of glacial acetic acid was warmed to 90°, 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°, $[\alpha]_D$ + 77° ($CHCl_3$), 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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