

Synthesis of Aziridinosteroids

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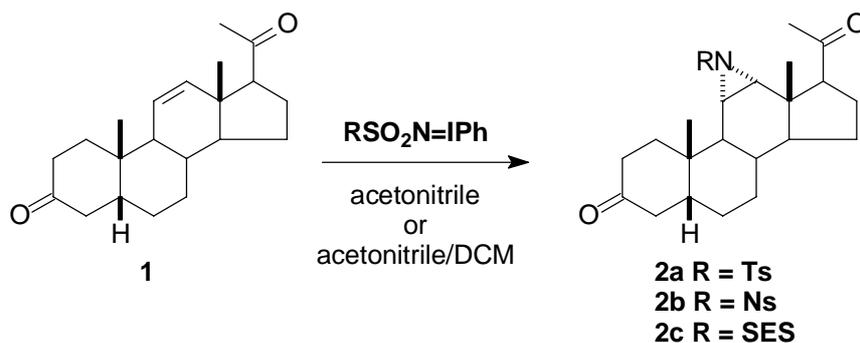
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Abstract: 11 α ,12 α -aziridinosteroids (**2a**, **b**, **c**) were prepared from 5 β -H-11-pregnene-3,20-dione (**1**) using different iminophenyliodines and chloramine aziridination reagents.

Introduction

The presence of a heteroatom, either replacing a methylene group of the steroid nucleus or as a substituent gives rise to major changes in the biological activity of steroid derivatives [1]. Thus, many steroidal nitrogen derivatives are pharmacologically important. Furthermore, 12 α -amino steroids have recently found application as chiral templates for combinatorial synthesis [2]. As an alternative way to introduce nitrogen functionalities into the steroid nucleus, we have explored the aziridination of steroidal double bonds. Aziridine ring opening with a nucleophile would yield aminosteroids with defined stereochemistry [3,4]. We describe the synthesis of 11 α ,12 α -aziridinosteroids (**2a**, **b**, **c**) by reaction of 11-pregnen-3,20-dione (**1**) with different aziridination reagents.



Experimental

Typical aziridination procedure: Copper (I) triflate (0.065 mmol) and 11-pregnen-3,20-dione (**1**, 0.65 mmol) were added under argon to a suspension of molecular sieves 4 Å (185 mg) in dry acetonitrile (1.65 ml). SES-iminophenyliodine (1.7 eq) was then added in 15 portions every 30 min with

vigorous stirring and stirring continued for 24 h at 25°C. The reaction mixture was filtered, evaporated to dryness and purified by column chromatography to yield **2c** (53% yield).

Results and Discussion

The aziridination reaction was carried out on several olefins (cyclohexene, styrene, norbornene, methyl acrylate, etc.) with a series of N-sulfonyl iminophenyl iodinanes and N-SES chloramine sodium salt and different catalysts (Cu (I) and Cu (II) triflate, PTAB, Py.HBr₃). With cyclohexene and (p-chlorobenzenesulfonyl)-iminophenyl iodinane the aziridine was obtained in 52% yield; cleavage with thiophenol followed by removal of the PhS group gave cycloheylamine in 95% yield.

Steroid **1** was treated with (tosylsulfonyl) and (nosylsulfonyl)-iminophenyl iodinane in acetonitrile-dichloromethane 1:1, rendering stereospecifically the 11 α ,12 α -aziridinosteroid (**2a, b**) with moderate yields (25-30%). Stereochemistry was established from the NOESY spectra (correlations H-19/H-11 β and H-18/H-12 β).

Attempts to aziridinate the 5,6 double bond in pregnenolone and pregnenolone acetate gave complex mixtures. On the other hand, the 4,5 conjugated double bond in progesterone was inert under the reaction conditions used.

To facilitate the deprotection step to give the free aziridine, (N-(2-trimethylsilyl)-ethanesulfonyl)-iminophenyl iodinane (PhI=NSES) was used as aziridination reagent. In this case, using acetonitrile as solvent, **1** rendered derivative **2c** in 53% yield. Aziridination of **1** with the sodium salt of (N-(2-trimethylsilyl)-ethanesulfonyl)-chloramine in acetonitrile gave **2c** in only 27% yield.

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References and Notes

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