A Novel Alkylation Reaction: Preparation of 3β-n-Butylcholestane

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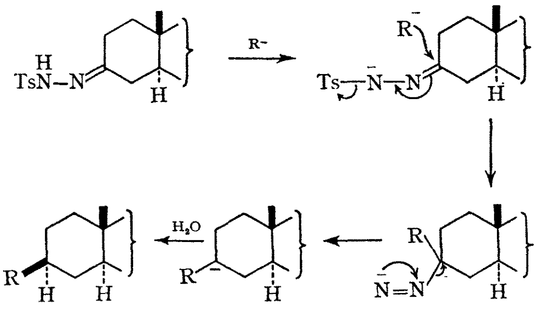
Summary 5α-Cholestan-3-one tosylhydrazone reacts with an excess of n-butyl-lithium to give 3β-n-butylcholestane instead of cholest-2-ene, which is obtained by reaction with stoicheiometric amounts of alkyl-lithiums.

RECENTLY, the preparation of olefins from tosylhydrazones by reaction with alkyl-lithium compounds has been described.[1-3] Applying this reaction to steroidal tosylhydrazones, we found the resulting olefins to be accompanied by varying amounts of monoalkylated steroidal hydrocarbons, depending on the excess of lithium alkyl used. A possible mechanism for this alkylation, similar to that suggested for the reaction of deuteriated metal hydrides with steroidal tosylhydrazones,[4] is shown in the next column.



SCHEME

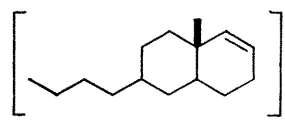
In a typical reaction, 5α-cholestan-3-one tosylhydrazone (1g) in anhydrous benzene (100 ml.) was cooled in an ice-bath, and 2N-n-butyl-lithium (50 ml.) (Aldrich) was added dropwise with stirring, under nitrogen. After 2 hr., the excess of butyl-lithium was destroyed by the addition of ice-water. The product was extracted into ether, and then chromatographed on silica gel impregnated with 25% silver nitrate. Butylcholestane was eluted with cyclohexane; m.p. 66°, $[\alpha]_D + 22°$, elemental analysis correct for $C_{31}H_{56}$.

The n.m.r. spectrum (100MHz.) showed the same peaks as 5α-cholestane in the region of 1 p.p.m., and in addition one small peak at 0·77 p.p.m., which can be ascribed to the triplet corresponding to the additional methyl group of the butyl residue. The mass spectrum of the n-butyl-5α-cholestane showed the following peaks, corresponding to all the main peaks of 5α-cholestane.[5]

To synthesize 3-n-butyl-5α-cholestane, a Wittig reaction with n-butyltriphenyl phosphonium bromide and 5α-cholestan-3-one was carried out. The product was hydrogenated over PtO_2 in EtOAc. The resulting n-butylcholestane was shown by gas chromatography to be a mixture of the 3β- and 3α-isomers. The major peak coincided with the product obtained from the alkylation reaction, which according to the above mechanism would be expected to be the more stable equatorial isomer. We are now investigating further the stereochemistry, scope, and limitation of this novel reaction.

M^+	428
$[M - (42 + C_6H_{17})]$	273
$[M - 15]^+$	413
$[M - C_8H_{17}]^+$	315
$[M - (C_8H_{17} + \text{Ring A})]$	259
Elision of Ring D	275

205



(*Received, September 12th,* 1969; *Com.* 1384.)

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