Synthesis of Steroidal 3,5-Dieno[3,4-*b*](5,6-dihydro-1,4-dithiins)[1]

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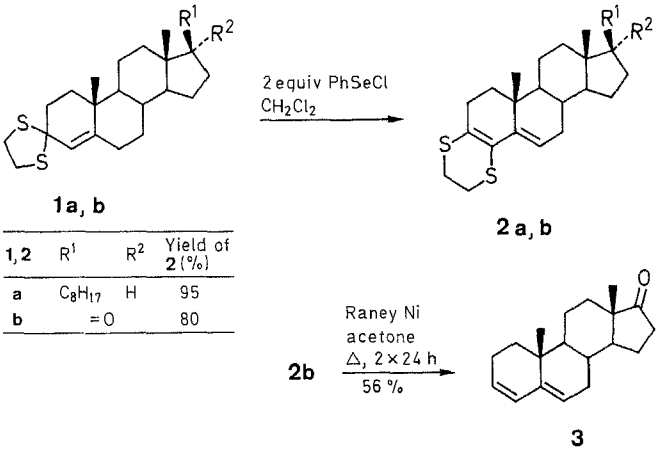
Reaction of steroidal 4-en-3-one ethylene dithioacetals with phenylselenenyl chloride in dichloromethane yields steroidal 3,5-dieno[3,4-*b*](5,6-dihydro-1,4-dithiins).

Steroidal 3,5-dieno[3,4-*b*](5,6-dihydro-1,4-dithiins)[3,4-(1,2-ethanedithio) steroid 3,5-dienes] have been synthesized via a number of methods.[2-4] We wish to report a new, one-step synthesis of steroidal 3,5-dieno[3,4-*b*](5,6-dihydro-1,4-dithiins) by oxidation of steroidal 4-en-3-one 3-spirocyclic ethylene dithioacetals with phenylselenenyl chloride. Reaction of cholest-4-en-3-one ethylene dithioacetal (**1a**) with two equivalents of phenylselenenyl chloride afforded cholesta-3,5-dieno[3,4-*b*](5,6-dihydro-1,4-dithiin) (**2a**) in 95% yield. The ultraviolet spectrum of **2a** exhibited two strong absorption bands at $\lambda_{max} = 240$ ($\varepsilon = 11490$) and 292 nm ($\varepsilon = 13300$) in agreement with those reported for cholesta-3,5-dieno[3,4-*b*](5,6-dihydro-1,4-dithiin) (**2a**).[2-4]

The C-3 ketone of androst-4-en-3,17-dione was selectively converted to the mono-dithioacetal **1b** using ethanedithiol in methanol with boron trifluoride as a Lewis acid catalyst.[5] Reaction of androst-4-en-3-one dithioacetal (**1b**) with two equivalents of phenylselenenyl chloride afforded 17-oxoandrosta-3,5-dien[3,4-*b*](5,6-dihydro-1,4-dithiin) (**2b**) in 80% yield. The structure of **2b** was based on spectral data. To conclusively prove its structure, **2b** was treated with Raney nickel to afford the desulfurized steroid, androsta-3,5-dien-17-one (**3**). This affords a convenient method for the conversion of a steroidal 4-en-3-one to a 3,5-diene.



1,2	R^1	R^2	Yield of 2 (%)
a	C_8H_{17}	H	95
b	=O		80

The mechanism of this ring expansion reaction can be rationalized as proceeding via a sulfenyl chloride intermediate[6] similar to the one reported for the reaction of spirocyclic ethylene dithioacetals with sulfuryl chloride.[7]

The reaction conditions described herein are much milder than those associated with the previous syntheses of the steroidal 3,5-dieno[3,4-*b*](5,6-dihydro-1,4-dithiins). This method should therefore prove to be superior for use with complex molecules containing labile functionality.

Cholesta-3,5-dieno[3,4-*b*](5,6-dihydro-1,4-dithiin) (2a):
To a cold (0–5°C) stirred solution of cholest-4-en-3-one ethylene dithioacetal (**1a**[8]; 1.5 g, 3.26 mmol) in CH_2Cl_2 (200 mL) is added dropwise over 15 min, PhSeCl (1.25 g, 6.52 mmol) in CH_2Cl_2 (50 mL). The solution is stirred for an additional 15 min, then poured into 5% aq. $NaHCO_3$ solution (50 mL), washed with water (50 mL), and dried ($MgSO_4$). Removal of the solvent gives **2a**, as a slightly yellow amorphous powder; yield: 1.41 g (95%). Purification is carried out by silica gel column chromatography (100 g) and eluting with 2% EtOAc in hexane; mp 156–159°C (CH_2Cl_2/MeOH) (Lit.[2] mp 165°C).

UV (CH_3CN): $\lambda_{max} = 240$ ($\varepsilon = 11490$), 292 nm ($\varepsilon = 13382$).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 0.70$ (s, 3H, CH_3-18); 0.87 (d, 6H, $J = 7$ Hz, CH_3-26 + CH_3-27); 0.98 (s, 3H, CH_3-19); 3.12 (s, 4H, SCH_2CH_2S); 5.88 (br m, 1H, $J = 11$ Hz, =CH).

Androsta-3,5-dieno[3,4-*b*](5,6-dihydro-1,4-dithiin) (2b):
4-Androstene-3,17-dione 3-ethylene dithioacetal (**1b**;[5] 4 g, 11 mmol) is oxidized with PhSeCl (4.23 g, 22 mmol) as described above, to afford **2b** after chromatography on silica gel (200 g); yield: 3.19 g (80%); mp 274–276°C (dec) (EtOAc/hexane, 1:3).

$C_{21}H_{28}OS_2$	calc.	C 69.61	H 7.96	S 17.74
(360.6)	found	69.97	7.83	17.76

UV (CH_3CN): λ_{max} = 240 (ε = 10205), 291 nm (ε = 11692).

IR (KBr): ν = 1730 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.89 (s, 3H, CH_3-18); 1.01 (s, 3H, CH_3-19); 3.15 (s, 4H, SCH_2CH_2S); 5.95 (m, 1H, =CH).

3,5-Androstadiene-17-one (3):
Raney nickel is prepared according to the method of Mozingo[9] and deactivated by refluxing in EtOAc and in acetone for 15 min each, before use. A mixture of **2b** (220 mg, 0.6 mmol) and deactivated Raney Nickel (2 g) in acetone (125 mL) is refluxed for 24 h. Then, more deactivated Raney nickel (1 g) is added and the mixture is refluxed for a further 24 h period. The mixture is filtered and concentrated *in vacuo* to yield an oily residue, which is chromatographed on silica gel (50 g) and eluated with 10% EtOAc in hexane to afford **3**; yield: 90 mg (56%); mp 83–85°C (Lit.[10] mp 85°C).

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(1) For the previous paper in this series see:
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