New digitalis steroids. Synthesis of 17α-amino 5β,14β-steroids by thermolysis of 17β-azidocarbonyloxymethyl derivatives

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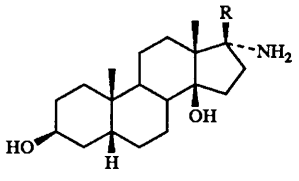
An efficient procedure for the synthesis of otherwise difficult to access 17α-amino derivatives of the digitalis series is described. The key reaction is the stereospecific thermocyclisation of 3β-acetoxy-17β-azidocarbonyloxymethyl-5β-androstan-14β-ol **3b** to (17*R*)-3β-acetoxy-14β-hydroxyspiro[5β-androstane-17,4'-oxazolidin]-2'-one **4**.

Natural cardiac glycosides, such as digoxin, digitoxin and ouabain, are well known drugs used for the treatment of congestive heart failure,[1] their pharmacological activity being mediated by inhibition of Na^+,K^+-ATPase.[2] As a part of a medicinal chemistry study, we wanted to introduce an amino substituent in the 17α position of the digitalis steroidal skeleton (general formula **1**) to study its influence on the binding of the



1 R = CH_2OH, CHO, CO_2H

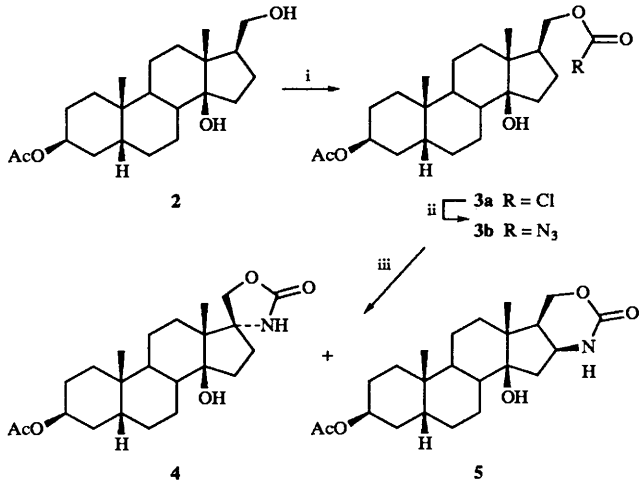
steroid to the Na^+,K^+-ATPase. No 17-amino derivatives of cardiac glycosides are known; only 3β- or 14β-amino derivatives have been described in the literature.[3]

17-Amino steroids, possessing a C/D *trans* ring junction, are classically prepared by Strecker reaction on 17-oxo derivatives, usually in high yields.[4] However, in our hands, using the same reaction conditions with the 17-oxo-5β-androstane-3β,14β-diol[5] and its 17-benzylimino derivative[6] did not lead to any reaction. An attempt to perform an α-amination on the 17β-formyl- as well as the 17β-carboxy-5β-androstane-3β,14β-diol with hydroxylamine-*O*-sulfonic acid[7] did not give any products.

It was felt that the approach of the reagents to the 17-carbon atom could be hampered by the steric hindrance of the vicinal quaternary carbon atom, associated with the C/D *cis* junction. We thus considered that an intramolecular reaction, where the reactant is forced to stay in close proximity to the 17α position, rather than an intermolecular one, would be a good strategy for a successful attack.

The photolysis or thermolysis[8] of acyl azides to acyl nitrenes was chosen as a suitable reaction for this purpose. It is known that CH-insertion by acyl nitrenes proceeds with retention of configuration,[8] and, therefore, a 17α-amino derivative was expected to be formed from a 17β-azidocarbonyloxymethyl substituent. The reactions shown in Scheme 1 were planned for testing this hypothesis.

Compound **2**[9] was treated with triphosgene to give the corresponding chloro carbonate **3a**, which was directly transformed into acyl azide **3b** by treatment with NaN_3 (72% overall yield). Thermolysis of **3b** in tetrachloroethane (140 °C, 1 h) gave the desired oxazolidinone **4** in 70% yield, together with the oxazinone by-product **5** (18%). The ratio of the two isomeric products **4** (oxazolidinone) and **5** (oxazinone) reflects the



Scheme 1 *Reagents and conditions:* i, triphosgene, pyridine, CH_2Cl_2, room temp.; ii, NaN_3, acetone, room temp.; iii, tetrachloroethane, 140 °C

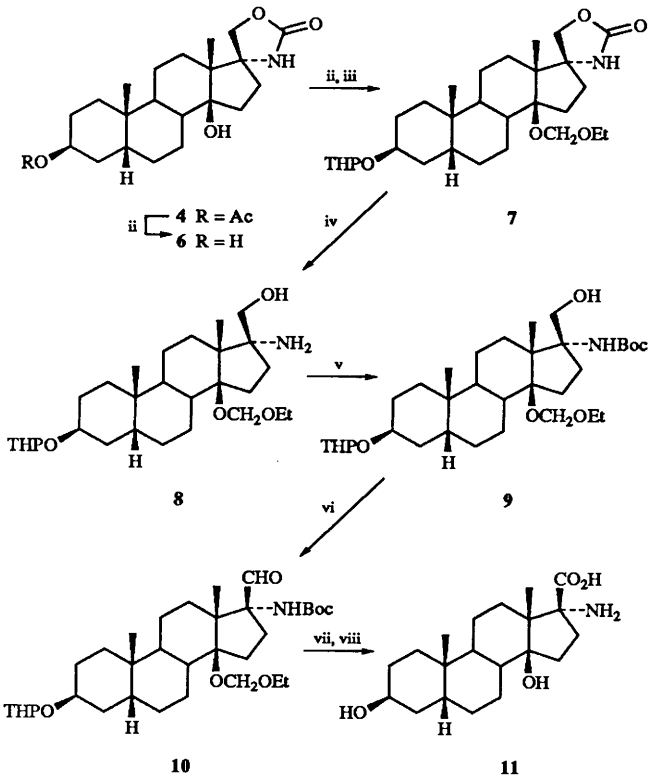
known preference of nitrenes to react with tertiary C–H bonds and to form five- *versus* six-membered rings.[8] The 17*R* absolute configuration of compound **4** was confirmed by the strong NOE observed between 13-Me and 20-H. The stereochemistry of compound **5** at C(16) was assigned on the basis of its chemical behaviour. In fact, under mild basic conditions (KOH, room temp., 72 h) urethane **5** undergoes an intramolecular transesterification with the 14β-OH. Thus, the relative stereochemistry of 14-OH and 16-NH groups must be *cis*.

Oxazolidinone **4** was then converted into the 14β-ethoxymethoxy ether **7**, which was quantitatively hydrolysed to amino alcohol **8** with KOH in ethanol (Scheme 2).

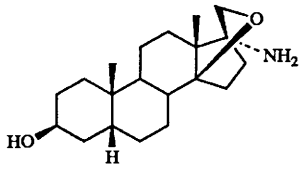
Amino alcohol **8**, after protection of the amino group as the Boc derivative, was oxidized to the corresponding aldehyde **10** with pyridinium dichromate and this was in turn converted into carboxylic acid **11** by $KMnO_4$ oxidation.

Direct hydrolysis of oxazolidinone **4** with KOH in EtOH at reflux did not give the desired 17α-amino-17β-hydroxymethyl compound, but led to ether **12**. The peculiar behaviour of urethane **4** towards basic hydrolysis, suggests that the 14β-hydroxy group is so close to C-20 that the intramolecular nucleophilic attack of the 14β-alcoholate on the urethane carbonyl group is preferred to intermolecular action of potassium hydroxide.

The displacement of the specific ^{3}H-ouabain binding from the Na^+,K^+-ATPase receptor, purified according to Jorgh-ensen[10] and Brown and Erdmann,[11] was evaluated to test the affinity of some of the new derivatives for the digitalis receptor.



Scheme 2 *Reagents and conditions:* i, KOH, EtOH, room temp.; ii, DHP, TsOH, dioxane, room temp.; iii, chloromethyl ethyl ether, DIPEA, CH_2Cl_2, reflux; iv, KOH, EtOH, reflux; v, Boc_2O, NaOH, Bu'OH, room temp.; vi, PDC, CH_2Cl_2, room temp.; vii, $KMnO_4$, NaH_2PO_4, Bu'OH, room temp.; viii, TsOH, MeCN–H_2O



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Compound **6** shows a weak but significant binding to Na^+,K^+-ATPase (IC_{50} = 1.0 × 10^{-5} mol dm^{-3}), while amino acid **11** possesses an IC_{50} value lower than 1.0 × 10^{-4} mol dm^{-3}.

Experimental

Mps were determined on a Büchi 535 apparatus and are uncorrected. IR spectra (KBr) were recorded on a Perkin-Elmer 1310 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained at 300.13 and 75.48 MHz respectively, on a Bruker AC-300 instrument. Chemical shifts are expressed in ppm (δ) downfield from tetramethylsilane (TMS) as internal standard. *J* Values are given in Hz. Multiplicity of carbon signals was determinated using the DEPT-135° experiment; all spectra were recorded in $CDCl_3$, unless otherwise specified. Mass spectra were obtained on an INCOS-50B Finnigan spectrometer in the DEP-EI mode at 70 eV. Elemental analyses were performed by Redox, Cologno Monzese, Italy. All reactions were carried out under a nitrogen atmosphere. Dichloromethane was dried over 4 Å molecular sieves. Purification by flash chromatography was performed according to the methodology of Still *et al.*[12]

3β-Acetoxy-17β-azidocarbonyloxymethyl-5β-androstan-14β-ol 3b

Triphosgene (5.7 g, 19.2 mmol) and pyridine (4.7 cm^3, 5.8 mmol) were added to a solution of the alcohol **2** (14 g, 38.5 mmol) in dry dichloromethane (540 cm^3). The reaction mixture was stirred for 3 h at room temperature, then a second portion of triphosgene (1.7 g, 5.8 mmol) was added and the reaction mixture stirred for 3 h. The organic solvent was evaporated under reduced pressure, the residue was dissolved in acetone (540 cm^3) and then sodium azide (12.5 g, 192 mmol) was added and the reaction mixture was stirred for 2 h at room temperature. The solid was filtered off, the solvent removed under reduced pressure and the residue purified by flash chromatography (cyclohexane–ethyl acetate, 85:15) to give the title compound **3b** (12 g, 72%), mp 144–146 °C (decomp.) (Found: C, 63.9; H, 8.25; N, 9.6. Calc. for $C_{23}H_{35}N_3O_5$: C, 63.7; H, 8.1; N, 9.7%); ν_{max}/cm^{-1} 3510, 2190, 2140, 1760 and 1730; δ_H 5.08 (1 H, m, 3-H), 4.42 (1 H, dd, *J* 6.7 and 11.2, CH*H*O), 4.27 (1 H, dd, *J* 8.2 and 11.2, C*H*HO), 2.06 (3 H, s, COMe) and 0.97 (6 H, s, 10-Me and 13-Me).

(17*R*)-3β-Acetoxy-14β-hydroxyspiro[5β-androstane-17,4'-oxazolidin]-2'-one 4 and (16*S*,17*R*)-3β-acetoxy-14β-hydroxy-3',6',16,17-tetrahydro-2'H-[1,3]oxazino[4',5':16,17]-5β-androstan-2'-one 5

A round bottomed flask containing a suspension of acyl azide **3b** (10.0 g, 23.1 mmol) in tetrachloroethane (800 cm^3) was placed in an oil bath preheated at 140 °C. The mixture was stirred for 1 h, until the evolution of nitrogen ceased. Tetrachloroethane was evaporated to dryness using the addition of propanol (4 × 200 cm^3) to make the evaporation easier. The solid residue was purified by flash chromatography (dichloromethane–ethyl acetate, 55:45) to give the title compounds **4** (6.58 g, 70%) and **5** (1.50 g, 18%).

For **4**: mp > 250 °C (Found: C, 68.25; H, 8.55; N, 3.5. Calc. for $C_{23}H_{35}NO_5$: C, 68.1; H, 8.7; N, 3.45%); ν_{max}/cm^{-1} 3490, 3280, 1740 and 1710; δ_H 6.11 (1 H, s, CONH), 5.08 (1 H, m, 3-H), 4.78 (1 H, d, *J* 9.5, CH*H*O), 4.15 (1 H, d, *J* 9.5, C*H*HO), 2.06 (3 H, s, COMe), 0.98 (3 H, s, Me) and 0.94 (3 H, s, Me).

For **5**: mp 241–244 °C (Found: C, 68.3; H, 8.5; N, 3.65. Calc. for $C_{23}H_{35}NO_5$: C, 68.1; H, 8.7; N, 3.45%); ν_{max}/cm^{-1} 3440 and 1715; δ_H 5.30 (1 H, br d, *J* 2.0, CONH), 5.08 (1 H, m, 3-H), 4.67 [1 H, dd, *J* 10.5 and 10.8, C(6')H*H*O], 4.17 [1 H, dd, *J* 5.7 and 10.8, C(20)*H*HO], 4.11 (1 H, dddd, *J* 2.0, 2.5, 8.8 and 9.0, 16-H), 2.49 [1 H, dd, *J* 9.0 and 15.0, C(15)H*H*], 2.26 (1 H, ddd, *J* 5.7, 8.8 and 10.5, 17-H), 2.06 (3 H, s, OCOMe), 1.82 [1 H, dd, *J* 2.5 and 15.0, C(15)*H*H], 1.02 (3 H, s, Me) and 0.95 (3 H, s, Me).

(17*R*)-3β,14β-Dihydroxyspiro[5β-androstane-17,4'-oxazolidin]-2'-one 6

Aqueous potassium hydroxide (4 mol dm^{-3}; 5 cm^3, 20 mmol) was added to a stirred solution of the acetate **4** (3.5 g, 8.64 mmol) in methanol (22 cm^3). After 24 h at room temperature, the solvent was evaporated and the residue triturated with water to give the title compound **6** (2.98 g, 95%), mp > 250 °C (Found: C, 69.2; H, 9.15; N, 3.65. Calc. for $C_{21}H_{33}NO_4$: C, 69.4; H, 9.15; N, 3.85%); ν_{max}/cm^{-1} 3440, 3260 and 1730; δ_H 5.10 (1 H, br s, CONH), 4.87 (1 H, d, *J* 9.5 CH*H*O), 4.16 (1 H, d, *J* 9.5, C*H*HO), 4.14 (1 H, m, 3-H), 0.97 (3 H, s, Me) and 0.94 (3 H, s, Me); δ_C(MeOD) 12.1 (q), 20.1 (t), 20.4 (t), 23.9 (q), 26.6 (t), 27.8 (t), 29.8 (2 C, t), 31.5 (t), 33.3 (t), 34.9 (t), 35.5 (s), 35.8 (d), 36.3 (d), 41.4 (d), 49.0 (s), 66.8 (d), 71.2 (s), 77.0 (t), 84.1 (s) and 160.8 (s); *m/z* 363 (M^+, 0.8%), 345 (3.5), 327 (5.4), 312 (9.2), 266 (16.9) and 251 (100).

(17*R*)-14β-Ethoxymethoxy-3β-[(*RS*)-tetrahydropyran-2-yloxy]spiro[5β-androstane-17,4'-oxazolidin]-2'-one 7

3,4-Dihydro-2*H*-pyran (DHP) (3.5 cm^3, 38.5 mmol) and toluene-*p*-sulfonic acid (PTSA) (10.5 mg, 0.055 mmol) were added to a stirred suspension of spiro compound **6** (1 g, 2.75

mmol) in dioxane (24 cm^3). After 18 h at room temperature, the reaction mixture was treated with 5% aq. sodium carbonate (5 cm^3) and then evaporated under reduced pressure. The residue was partitioned between ethyl acetate and water. The organic layer was dried over sodium sulfate and the solvent evaporated to dryness under reduced pressure. Flash chromatography of the residue (ethyl acetate–dichloromethane, 55:45) gave (17*R*)-14β-hydroxy-3β-[(*RS*)-tetrahydropyran-2-yloxy]-spiro[5β-androstane-17,4′-oxazolidin]-2′-one (1.17 g, 95%) (Found: C, 70.0; H, 9.35; N, 3.0. Calc. for $C_{26}H_{41}NO_5$: C, 69.8; H, 9.2; N, 3.1%); δ_H 5.88 and 5.81 (1 H, 2 × br s, CONH), 4.86 (1 H, d, *J* 9.5, CH*H*CON), 4.62 (1 H, m, OCHO), 4.15 (2 H, d, *J* 9.5, C*H*HOCON), 3.96 (1 H, m, 3-H), 3.95–3.40 (2 H, m, CH_2O), 0.98 (3 H, s, Me) and 0.94 (3 H, s, Me).

Chloromethyl ethyl ether (7.3 cm^3, 78.3 mmol) was added dropwise over 20 min to a stirred solution of (17*R*)-14β-hydroxy-3β-[(*RS*)-tetrahydropyran-2-yloxy]-spiro[5β-androstane-17,4′-oxazolidin]-2′-one (3.5 g, 7.83 mmol) and diisopropylethylamine (DIPEA) (33.5 cm^3, 196 mmol) in dry dichloromethane (130 cm^3) at 0 °C. The reaction solution was refluxed overnight and then cooled and diluted with ethyl acetate (100 cm^3). The organic phase was washed with 5% aq. citric acid (5 × 20 cm^3) and water (3 × 20 cm^3) and dried over sodium sulfate. The solvent was removed under reduced pressure. The residue was purified by chromatography (chloroform–ethyl acetate, 65:35) to give the title compound **7** (3.05 g, 77%), mp 76–83 °C (Found: C, 68.7; H, 9.2; N, 3.0. Calc. for $C_{29}H_{47}NO_6$: C, 68.9; H, 9.4; N, 2.8%); ν_{max}/cm^{-1} 3280 and 1700; δ_H 5.79 and 5.75 (1 H, two br s, CONH), 4.83 (1 H, d, *J* 7.0, OCH*H*O), 4.81 (1 H, d, *J* 9.5, CH*H*OCON), 4.71 (1 H, d *J* 7.0, OC*H*HO), 4.65 (1 H, m, OCHO), 4.19 (1 H, d, *J* 9.5, C*H*HOCON), 3.95 (1 H, m, 3-H), 3.95–3.40 (4 H, m, OCH_2CH_3 and OCH_2CH_2), 1.21 (3 H, t, *J* 7.0, OCH_2CH_3), 1.03 (3 H, s, Me) and 0.94 (3 H, s, Me).

17α-Amino-14β-ethoxymethoxy-17β-hydroxymethyl-3β-[(*RS*)-tetrahydropyran-2-yloxy]-5β-androstane 8

Potassium hydroxide (6.68 g, 119 mmol) was added to a solution of urethane **7** (3.0 g, 5.94 mmol) in ethanol 90% (80 cm^3). The reaction mixture was refluxed for 8 h and then stirred overnight at room temperature. The solvent was evaporated and the residue diluted with chloroform. The organic phase was washed with 1 mol dm^{-3} hydrochloric acid and with water, dried over sodium sulfate and evaporated to dryness. Flash chromatography of the residue (chloroform–methanol–ammonia, 90:10:1) gave the title compound **8** (2.3 g, 81%) as an amorphous solid (Found: C, 70.4; H, 10.1; N, 3.1. Calc. for $C_{28}H_{49}NO_5$: C, 70.1; H, 10.3; N, 2.9%); ν_{max}/cm^{-1} 3420 and 3215; δ_H 4.84 (1 H, d, *J* 7.0, OCH*H*O), 4.72 (1 H, d, *J* 7.0, OC*H*HO), 4.63 (1 H, m, OCHO), 3.95 (1 H, m, 3-H), 3.79 (1 H, d, *J* 13.8, CH*H*OH), 3.95–3.40 (4 H, m, OCH_2CH_3 and OCH_2CH_2), 3.36 (1 H, d, *J* 13.8, C*H*HOH), 1.20 (3 H, t, *J* 7.0, OCH_2CH_3), 0.96 (3 H, s, Me) and 0.87 (3 H, s, Me).

17α-*tert*-Butoxycarbonylamino-14β-ethoxymethoxy-17β-hydroxymethyl-3β-[(*RS*)-tetrahydropyran-2-yloxy]-5β-androstane 9

A mixture of the amino alcohol **8** (2.3 g, 4.80 mmol), aqueous sodium hydroxide (1 mol dm^{-3}; 7.9 cm^3, 7.9 mmol) and di-*tert*-butyl dicarbonate (1.57 g, 7.20 mmol) in *tert*-butyl alcohol (90 cm^3) was stirred at room temperature for 48 h. The solution was then diluted with ethyl acetate, the organic layer washed with 5% aq. sodium dihydrogen phosphate and water, dried over sodium sulfate and evaporated to dryness under reduced pressure. Flash chromatography of the residue (dichloromethane–ethyl acetate, 75:25) gave the title compound **9** (2.55 g, 92%) as an amorphous solid (Found: C, 68.25; H, 10.15; N, 2.3. Calc. for $C_{33}H_{57}NO_7$: C, 68.4; H, 9.9; N, 2.4%); ν_{max}/cm^{-1} 3430 and 1690; δ_H 4.85 (1 H, d, *J* 7.0, OCH*H*O), 4.72 (1 H, d, *J* 7.0, OC*H*HO), 4.63 (2 H, m, OCHO and NHCO), 4.13 (1 H, d, *J* 13.8, CH*H*OH), 3.95 (1 H, m, 3-H), 3.88 (1 H, d, *J* 13.8, C*H*HOH), 3.95–3.40 (4 H, m, OCH_2CH_3 and OCH_2CH_2), 1.18 (3 H, t, *J* 7.0, OCH_2CH_3), 1.45 (9 H, s, CO_2Bu^t), 1.08 (3 H, s, Me) and 0.95 (3 H, s, Me).

17α-*tert*-Butoxycarbonylamino-14β-ethoxymethoxy-3β-[(*RS*)-tetrahydropyran-2-yloxy]-5β-androstane-17β-carbaldehyde 10

A mixture of the alcohol **9** (1 g, 1.73 mmol), pyridinium dichromate (PDC) (910 mg, 2.43 mmol) and 4 Å molecular sieves (1.73 g) in dry dichloromethane (15 cm^3) was stirred at room temperature for 28 h. The mixture was filtered through a pad of Celite–silica gel, washed with ethyl acetate and the filtrate evaporated to dryness. The residue was purified by flash chromatography (cyclohexane–ethyl acetate, 85:15) to give the title compound **10** (800 mg, 80%), mp 74–80 °C (Found: C, 68.8; H, 9.45; N, 2.55. Calc. for $C_{33}H_{55}NO_7$: C, 68.6; H, 9.6; N, 2.4%); ν_{max}/cm^{-1} 3370 and 1715; δ_H 9.61 (1 H, s, CHO), 5.05 (1 H, br s, NHCO), 4.80 (1 H, d, *J* 7.0, OCH*H*O), 4.69 (1 H, d, *J* 7.0, OC*H*HO), 4.63 (1 H, m, OCHO), 3.98 (1 H, m, 3-H), 3.95–3.40 (4 H, m, OCH_2CH_3 and OCH_2CH_2), 1.45 (9 H, s, CO_2Bu^t), 1.21 (3 H, t, *J* 7.0, OCH_2CH_3), 0.96 (3 H, s, Me) and 0.94 (3 H, s, Me).

17α-Amino-3,14β-dihydroxy-5β-androstane-17β-carboxylic acid 11

Sodium dihydrogen phosphate (1.25 mol dm^{-3}; 3.5 cm^3, 4.33 mmol) and potassium permanganate (1 mol dm^{-3}; 5.2 cm^3, 5.20 mmol) were added under vigorous stirring to a solution of the aldehyde **10** (500 mg, 0.866 mmol) in *tert*-butyl alcohol (5 cm^3) and the mixture was stirred at room temperature for 2.5 h. 5% Aqueous $NaHSO_3$ (10 cm^3) was added to the mixture which was then stirred for 30 min before hydrochloric acid (0.1 mol dm^{-3}) was added and the mixture extracted with ethyl acetate. The organic phase was washed with water, dried over sodium sulfate and evaporated to dryness. Flash chromatography (cyclohexane–ethyl acetate, 6:4) of the residue gave 17α-*tert*-butoxycarbonylamino-14β-ethoxymethoxy-3β-[(*RS*)-tetrahydropyran-2-yloxy]-5β-androstane-17β-carboxylic acid (390 mg, 75%) (Found: C, 66.9; H, 9.15; N, 2.55. Calc. for $C_{33}H_{55}NO_8$: C, 66.75; H, 9.3; N, 2.4%); δ_H 5.63 (1 H, br s, CONH), 4.98 (1 H, d, *J* 7.0, OCH*H*O), 4.72 (1 H, d, *J* 7.0, OC*H*HO), 4.63 (1 H, m, OCHO), 3.97 (1 H, m, 3-H), 3.95–3.40 (4 H, m, OCH_2CH_3 and OCH_2CH_2), 1.45 (9 H, s, CO_2Bu^t), 1.21 (3 H, t, *J* 7.0, OCH_2CH_3), 1.03 (3 H, s, Me) and 0.94 (3 H, s, Me); *m/z* 548 (0.1%), 509 (0.1), 458 (8.5), 402 (20.3), 390 (18.3) and 57 (100).

A mixture of 17α-*tert*-butoxycarbonylamino-14β-ethoxymethoxy-3β-[(*RS*)-tetrahydropyran-2-yloxy]-5β-androstane-17β-carboxylic acid (390 mg, 0.657 mmol) and PTSA (100 mg, 0.52 mmol) in acetonitrile–water (85:15; 50 cm^3) was refluxed for 3 h, the mixture was then cooled and evaporated under reduced pressure. The residue was chromatographed (chloroform–methanol–ammonia from 80:20:2 to 70:30:2) to give the title amino acid **11** (145 mg, 60%), mp > 250 °C (Found: C, 68.15; H, 9.8; N, 3.85. Calc. for $C_{20}H_{33}NO_4$: C, 68.3; H, 9.5; N, 4.0%); ν_{max}/cm^{-1} 3100–2700 and 1660; δ_H(MeOD) 4.04 (1 H, m, 3-H), 1.08 (3 H, s, Me), 0.97 (3 H, s, Me); δ_C(MeOD) 14.6 (q), 21.9 (t), 22.1 (t), 24.3 (q), 27.7 (t), 28.5 (t), 30.7 (t), 32.4 (t), 33.6 (t), 33.9 (t), 34.2 (t), 36.1 (d), 36.3 (s), 37.3 (d), 42.1 (d), 50.8 (s), 67.6 (d), 75.5 (s), 86.2 (s) and 177.6 (s); *m/z* 333 (3.2%), 316 (5.8), 306 (4.4), 298 (2.7), 288 (6.2) and 274 (100).

(14*R*,17*R*)-17α-Amino-14,17-epoxymethano-5β-androstan-3β-ol 12

Potassium hydroxide (3.45 g, 61.5 mmol) was added to a stirred solution of urethane **4** (0.5 g, 1.23 mmol) in ethanol 90% (11 cm^3). The mixture was refluxed for 4 h. The solvent was

evaporated and the residue diluted with ethyl acetate. The organic phase was washed with hydrochloric acid (1 mol dm^{-3}) and with water, dried over sodium sulfate and evaporated. Flash chromatography of the residue (chloroform–methanol, 80:20) gave the title compound **12** (212 mg, 51%) mp 162–165 °C (Found: C, 75.35; H, 10.6; N, 4.25. Calc. for $C_{20}H_{33}NO_2$: C, 75.2; H, 10.4; N, 4.4%); ν_{max}/cm^{-1} 3330, 3280 and 3200; δ_H 4.12 (1 H, m, 3-H), 3.59 [1 H, dd, *J* 3.0 and 8.0, C(20)H*H*O], 3.52 [1 H, d, *J* 8.0, C(20)*H*HO], 1.02 (3 H, s, Me) and 0.88 (3 H, s, Me); δ_C([$^2H_6$]DMSO) 12.9 (q), 19.9 (t), 21.0 (t), 23.8 (q), 26.5 (t), 27.2 (t), 27.9 (t), 27.9 (t), 29.0 (t), 30.7 (t), 33.8 (t), 35.3 (d), 35.7 (s), 36.4 (d), 36.6 (d), 47.7 (s), 63.9 (s), 65.9 (d), 72.7 (d) and 89.1 (s).

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