Azasteroids derived from fusidic acid

William S. Murphy,*[a] Basil Sarsam,[a] George Ferguson[b] and John F. Gallagher[b]

[a] *Department of Chemistry, National University of Ireland, Cork, Ireland*
[b] *Department of Chemistry and Biochemistry, University of Guelph, Guelph, Ontario, Canada, NIG 2W1*

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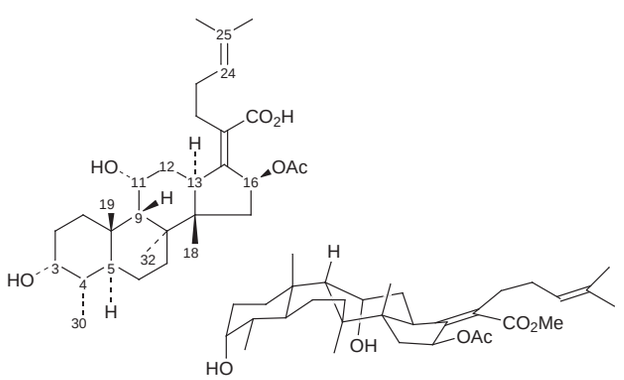
The Beckmann rearrangement pathway of the (*E*)-11-oxime **6**, derived from fusidic acid, one of the uncommon 9β-steroids with ring B constrained in a boat conformation, was investigated. It was found that **6** was converted into methyl 3-*O*-acetyl-11-aza-11a-homo-11a-oxo-24,25-dihydrofusidate **7**, the 'normal' product of rearrangement, when treated with toluene-*p*-sulfonyl chloride in pyridine. The structure and stereochemistry of **7** was determined by X-ray crystallography. The absolute configuration of fusidic acid was confirmed. The Beckmann rearrangement of the oxime derivatives of 3- and 17-oxo-9β-steroids derived from fusidic acid was also investigated. In general, with the exception of the (*E*)-oxime of 17-oxotriacetate **13b**, which resulted in a complex mixture of products, none of which predominated, all the oximes gave the normal Beckmann rearrangement products.

Fusidic acid[1] **1** is a natural steroidal antibiotic. In this cyclopentanoperhydrophenanthrene ring system, ring B is forced into a strained boat conformation by the *trans-syn-trans* fusion of the A, B and C rings, respectively. In a number of chemical reactions[2a,b] involving this system, unexpected rearrangements involving a 1,2-shift of the 8α-methyl group were observed. The driving force for these reactions was largely relief of the strain associated with the enforced boat conformation of ring B. In this present investigation, the Beckmann rearrangement[3] of the oxime derivatives of 3-, 11- and 17-oxo-9β-steroids derived from fusidic acid was investigated for the following reasons: (a) to determine whether the oxime derivatives of these uncommon 11-oxo-9β-steroids would undergo normal *anti*-Beckmann rearrangement or an alternative more deep-seated, strain-relieving rearrangement and (b) to develop a facile entry into novel classes of azasteroids with potential biological activity. Azasteroids are of continuing interest due to their biological and medicinal properties.[4] Also oxosteroids[5a–e] derived from fusidic acid have exhibited biological activity. The oximes of the oxosteroids **2**–**5** were selected for this study.



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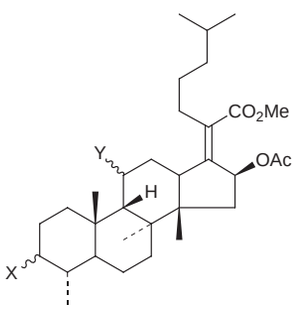
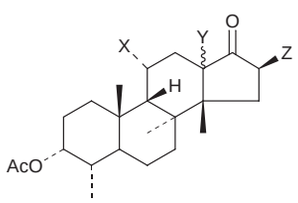
Beckmann rearrangements of oxosteroid oximes have been investigated previously. These investigations have been largely confined to rings A[6] and D[7] ketoximes although there have been investigations of both ring B[8] and ring C[9] ketoximes. In general, the substrates have been 'normal' and did not have any unusual inherent strain as that found in the 9β fusidic acid nucleus. The products in general have been those predicted on the basis of the group *anti* to the leaving group migrating with retention of configuration.[10]



2 X = α-AcO, Y = O=
3 X = O=, Y = α-HO



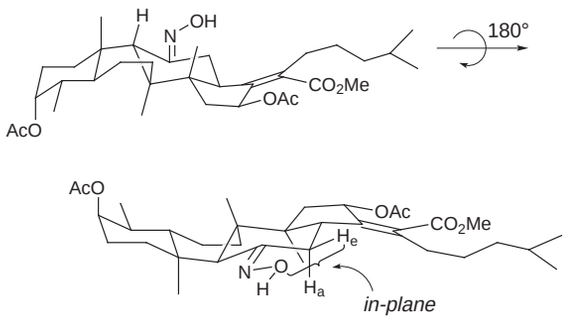
4 X = AcO, Y = α-H, Z = AcO
5 X = Z = H, Y = β-H

Results and discussion

Investigation of the Beckmann rearrangement of the C-11 oxime

The known methyl 3*α*-*O*-acetyl-11-oxo-24,25-dihydrofusidate **2** was synthesised using slight modifications of literature procedures.[11,12] The oxime of this keto ester was prepared by heating it under reflux with a large excess of hydroxylamine hydrochloride and potassium acetate.[13] Only the (*E*)-oxime **6** was detected, with no evidence for the formation of the (*Z*)-isomer. The stereochemistry of this oxime was established by NMR. The one proton doublet of doublets at δ 3.94 ppm was assigned as the 12α-H (equatorial) proton. A signal at this low field was almost certainly due to the deshielding anisotropic effect of the in-plane oxygen of the (*E*)-oxime group.[14a,b] Thus determination of the stereochemistry of the oxime functionality depended on the unambiguous assignment of the 12α-H (equatorial) proton. This assignment was confirmed by the multiplicity and magnitude of the coupling constants, J 4.7 and 13.9 Hz; the latter coupling constant is that resulting from *gem*-coupling and the former, the vicinal coupling between the 12α-H equatorial proton and the 13-H (axial) proton. On the basis of the Karplus curve, this represents a dihedral angle of approximately 52° between these two protons[15] and is consistent with the assignment of the structure as **6** (Scheme 1).

Additional evidence for the assignment of 12*α*-H (equatorial)



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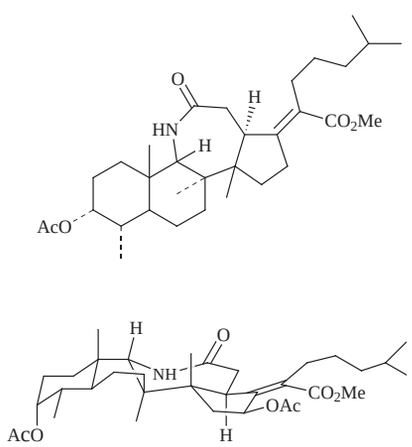
Scheme 1

was obtained by NMR selective decoupling. There is a two proton multiplet at δ 2.64 ppm in the ^{1}H NMR spectrum of the oxime **6**. ^{13}C{^{1}H}-Selective spin decoupling was used to assign one of these as the axial 13-H proton. By irradiating this multiplet at δ 2.64 ppm, the doublet at δ_C 46.34 collapsed to a singlet in the ^{13}C NMR spectrum. This doublet corresponded to 13-H on the basis of multiplicity and by correlation with a series of related compounds. This 13-H proton was then decoupled from the 12α-H. The doublet of doublets at δ_H 3.94 then collapsed to a doublet, with J equal to 13.9 Hz. This result confirms the assignment of the chemical shift of 12α-H and confirms that the magnitude of the downfield shift to δ_H 3.94 is a consequence of the deshielding of the oxime group with (*E*)-stereochemistry.

The (*E*)-oxime **6** was treated with toluene-*p*-sulfonyl chloride in pyridine at 20 °C for 13 days.[3] The product **7** was isolated



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after dry flash chromatography in 81% yield. This product was confirmed as a lactam both by the presence of absorbances in the IR spectrum at 3320 and 1635 cm^{-1} and by the presence of an amide carbonyl signal at δ_c 174.39 in the ^{13}C NMR spectrum.

In the ^{1}H NMR spectrum of the lactam **7**, the doublet at δ_H 5.82 disappeared and the doublet at δ_H 3.61 collapsed to a singlet when the sample was shaken with deuteriated water. As a consequence, 9-H was assigned the chemical shift δ_H 3.61. This chemical shift provided strong evidence that the lactam had the structure **7**, since insertion of nitrogen on the other side of the carbonyl group in ring C would otherwise have resulted in 9-H with a chemical shift approximately the same as in the ketone **2** or in oxime **6** *i.e.* approximately δ_H 2.5.

Further confirmatory evidence for the assignment of structure **7** was obtained from high field NMR data. The doublet at δ 3.0 was assigned to the axial 13-H proton and the quintet at

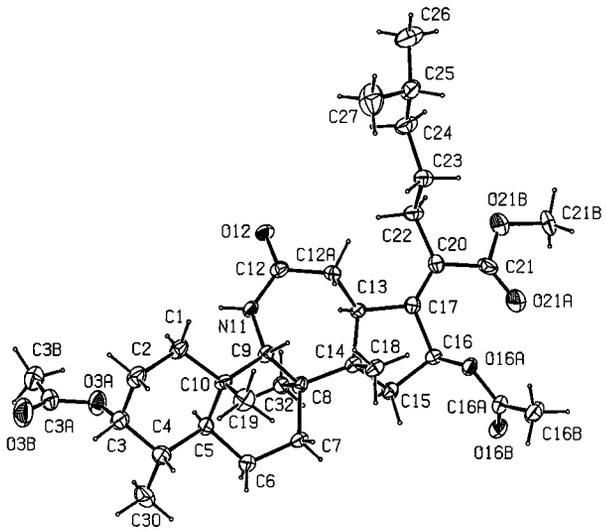


Fig. 1 A view of molecule **7** with the numbering scheme (chosen on chemical grounds). Anisotropic displacement parameters are drawn at the 20% level. Only one of the two orientations of the disordered ester group is shown.

δ 2.80 to the two C-12 protons. These assignments were confirmed by ^{1}H decoupling experiments: double irradiation at δ 2.80 resulted in the collapse of the quintet to a broad singlet and double irradiation at δ 3.0 resulted in the collapse of the doublet at δ 2.80 to a singlet. The chemical shift of 12-H is consistent with the structural assignment, **7**.

NOE difference spectroscopy was employed in an attempt to determine the configuration at C-9. If the 9-H proton had a β-configuration, then NOE enhancement could be expected as a consequence of irradiating the C-19 methyl protons. By correlation with a series of related fusidanes, this methyl (C-19) was assigned the chemical shift δ 1.14 *viz a viz* the proximate methyl singlet at δ 1.13. In the event, it proved impossible to double irradiate the singlet at δ 1.14 specifically. The adjoining singlet was also affected. The C-9 proton exhibited a positive NOE enhancement (12.1%). However, this result was ambiguous since in effect both singlets were doubly irradiated. The singlet at δ 1.13 corresponded to the C-32 methyl group; if C-9 had the α-configuration, then double irradiation at the latter frequency would likewise be expected to result in an NOE enhancement. In effect, the configuration of C-9 remained uncertain. Structure elucidation was therefore undertaken by X-ray crystallography.

The structure, stereochemistry and absolute configuration of the lactam **7** were determined by X-ray crystallography and are represented in Fig. 1 (for details of the X-ray analysis, see the Experimental section). The crystal structure contains discrete molecules linked into chains *via* intermolecular N11–H···O16B* hydrogen bonds (N···O 3.187(8) Å); other intermolecular contacts correspond with normal van der Waals interactions.

The conformations of the fused rings in **7** are as follows: ring A has a chair conformation, ring B is a twist boat, the 7-membered N-containing ring C has a chair conformation (N11 and C12 below and C14 above the plane of C8, C9, C11a, C13), ring D has an envelope conformation with C14 0.63(3) Å out of the C13, C15, C16, C17 plane. Molecular dimensions are unexceptional and serve to establish the structure unequivocally, they are available with the supplementary material.

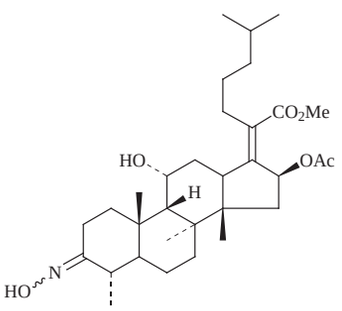
A search of the Cambridge Structural Database[16] for structures using only the non-hydrogen atoms of the four fused ring skeleton revealed that no structures of this type have previously been reported. A similar search without the carbonyl oxygen O3 atom and changing the N chemical type to C yielded only two structures. These are (+)-17β-acetoxy-3-methoxy-C-homo-9β-estra-1,3,5(10)-triene[17] and (13*S*)-17α-methyl-12a-

methylene-C(12a)-homo-18-norandrost-5-en-3β-yl acetate.[18] The structures found in this search differ significantly from the present structural determination and serve to indicate the paucity of structures of this general structural type.

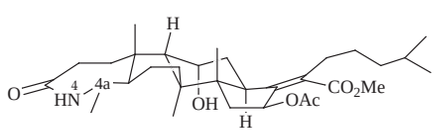
It is clear from the X-ray analysis, that 9-H in the lactam **7** has the β-configuration. It follows that the Beckmann rearrangement of the (*E*)-oxime **6** occurred in the expected manner, *i.e.* that the substituent *anti* to the oxime group migrated and with retention of configuration. As a corollary, (*E*)–(*Z*) isomerisation of the C-11 oxime group in **6** apparently did not occur under the experimental conditions. This result contrasts sharply with the behaviour of the C-3 group (see below).

Investigation of the Beckmann rearrangement of the C-3 oximes

The 3-oxoester **3** required for this study was synthesised from methyl 24,25-dihydrofusidate[11] by an alternative method[19] of regioselective oxidation using *N*-bromosuccinimide in aqueous dioxane.[20] Treatment of this ketone **3** with hydroxylamine hydrochloride in methanol at 20 °C with potassium acetate, resulted in a quantitative conversion to an (*E*)–(*Z*)-mixture of oximes, **8a** and **8b**, in 90 min, at room temperature. The rate



8a (*E*) - configuration
8b (*Z*) - configuration



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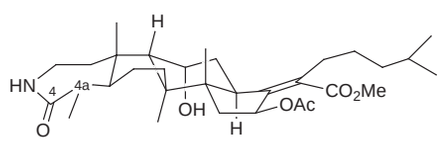
of this reaction is strikingly greater than the corresponding reaction of the 11-ketone **2**, probably for steric reasons.[21] The ratio of stereoisomers, which were separated chromatographically, varied between 6:1 and 10:1, respectively. The stereoisomers were readily assigned by ^{1}H NMR on the basis of chemical shift due to deshielding of the in-plane equatorial proton, together with signal multiplicity. Thus the major (*E*)-isomer **8a** was assigned on the basis that the 2α-H (equatorial) proton was deshielded and thus observed at low field as a multiplet centred at δ_H 3.24. The **8b** isomer had no corresponding signal. This stereochemical assignment was confirmed by doubly irradiating the multiplet at δ_H 3.24 in the NMR spectrum of the major oxime, **8a**. The doublet at δ_H 1.10 due to the C-4 methyl group was unaffected. Conversely, when the signal at δ_H 1.10 was doubly irradiated, the multiplet at δ_H 3.24 remained unaffected.

The major isomer **8a** was treated with toluene-*p*-sulfonyl chloride in pyridine at 20 °C for 102 h. The product isolated in 62.5% was confirmed as a lactam, by the strong absorptions in the IR spectrum at 3400 and 1650 cm^{-1} and by the presence of a carbonyl singlet at δ_C 176.70 in the ^{13}C NMR spectrum. In the ^{1}H NMR spectrum the broad multiplet at δ_C 3.40 collapsed to a broad quintet and the doublet at δ_H 6.0 disappeared when the sample was treated with deuteriated water. These signals corresponded therefore to the CHMe group and the adjoining NH, respectively. Spin decoupling *in situ* of this deuteriated sample was undertaken at the doublet at δ_H 1.2 and resulted in the conversion of the multiplet at δ_H 3.4 to a doublet (*J* 8.6 Hz). This coupling constant is consistent with a dihedral angle of approximately 180°. Thus, 4β-H is axial and *trans* to 5α-H. Therefore, C-4 had migrated and with retention of configuration in the course of the rearrangement of the (*E*)-oxime **8a**. This lactam rearrangement product is assigned the structure **9**. We may conclude that no (*E*)–(*Z*) isomerisation of the oxime had occurred under the reaction conditions.[22]

The minor (*Z*)-oxime **8b** was similarly treated with toluene-*p*-sulfonyl chloride in pyridine at 20 °C for 102 h. The lactam product was isolated in 57% yield. In order to avoid isomerisation, the oxime **8b** was not purified by recrystallisation.[22] However, in this instance when the reaction mixture was analysed by thin layer chromatography before completion of the reaction, it was noted the oxime **8b** had isomerised into a mixture of (*E*)- and (*Z*)-isomers.[22] Predictably two lactams were formed, which we failed to separate. However, unequivocal evidence for the composition of the mixture was obtained from the ^{1}H NMR specrum. In addition to the signals due to the lactam **9** were those consistent with the lactam **10**, present in an approximately 1:1 ratio.

The assignment of structure **10** follows, *inter alia*, from the



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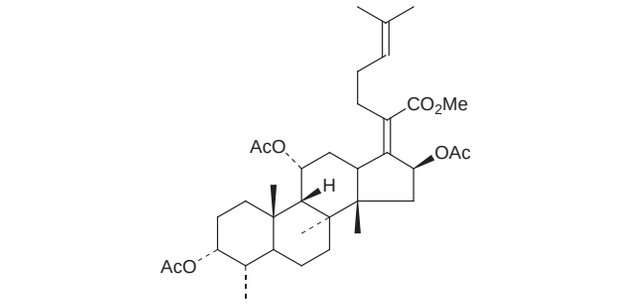
presence of the one-proton doublet of multiplets at δ_H 3.22 which changed to a doublet of triplets when shaken with deuteriated water and represents the pseudo-equatorial proton at C-2, *J* 16.9 and 4.2 Hz. The coupling constant *J* 16.9 Hz is due to the geminal coupling at C-2. The second coupling constant *J* 4.2 Hz is consistent with equal coupling between 2α-H and the vicinal protons at C-1.

Investigation of the Beckmann rearrangement of the C-17 oximes

Methyl bis-*O*-acetylfusidate **11**[23,24] was oxidised to the 17-ketone **4**[25,26] in good yield with ruthenium tetroxide, using the Sharpless modification.[27] A side-product, **12**, was formed in 10% yield. The latter was assigned on the basis of OH and CO stretching frequency absorbtions at 1775 and 3450 cm^{-1} and the quaternary carbons at δ_C 176.24, 85.37 and 85.17. The lactone **12** is considered to arise *via* glycol formation on the less hindered α-face[28] of the respective acid followed by spontaneous lactonisation under the acidic work-up conditions.

The ketone **4** was converted to a 1:1 mixture of (*E*)- and (*Z*)-oximes by treatment with hydroxylamine hydrochloride and potassium acetate in methanol at 20 °C for 2 d. The oximes were separated by flash chromatography. The configurations of the oximes were assigned on the basis of the magnitude of the change in the chemical shift of the doublet assigned as 16-H relative to that in the parent ketone **4**. The less polar oxime was assigned the (*Z*)-configuration **13a**, since it exhibited the larger downfield shift ($\Delta\delta$ = 0.65 ppm) compared with the more polar (*E*)-oxime, **13b** ($\Delta\delta$ = 0.21 ppm).

In the ^{1}H NMR spectrum of **13a** there is a doublet of doublets at δ_H 2.78 ($J_{12\beta,13}$ 11.4 and $J_{12\alpha,13}$ 2.8 Hz) which corresponds to an α (axial) configuration at C-13. Careful analysis permitted the assignment of the stereochemistry of C-13 in **13b**, also as the α-configuration. Assignment was made difficult by overlap of one half of each of the multiplets corresponding to 13-H and 12α-H. The 13-H proton, at δ_H 2.84, is observed as a doublet of doublets ($J_{12\beta,13}$ 12.98 and $J_{12\alpha,13}$ 3Hz). The 12α-H proton,



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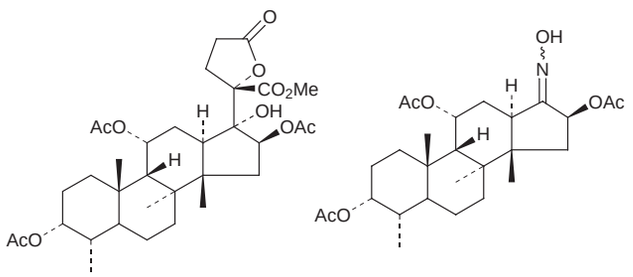

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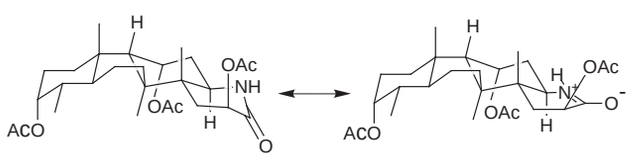
13 a (*Z*) - configuration
13 b (*E*) - configuration



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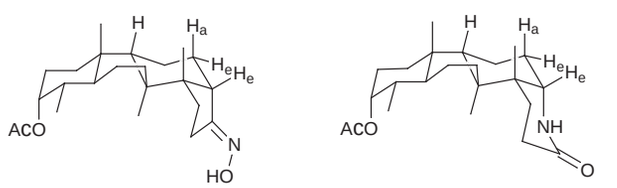

15 16

at δ_H 2.78 is a doublet of triplets (J_{gem} 14.65, $J_{11,12\alpha} = J_{12\alpha,13}$ 3Hz). Thus both of the oximes **13a** and **13b** have a CD *trans*-fused configuration, the same as in the parent ketone **4**. The stereochemistry at C-13 was not affected in the course of formation of both oximes.

The (*Z*)-oxime **13a**, was treated with tosyl chloride in pyridine and after a protracted period (12 days) at 20 °C, the reaction was complete. The Beckmann rearrangement product **14**, was isolated and readily confirmed as a lactam by IR and ^{13}C NMR spectroscopy. In the ^1H NMR spectrum, there was a doublet of doublets at δ_H 3.84 which was assigned as the axial proton at C-13. The coupling constants $J_{12\beta,13} = 11.8$ Hz and $J_{12\alpha,13}$ 4.7 Hz are consistent[14] with coupling between the axial 13-H and the axial and equatorial protons on C-12, respectively. The multiplet at δ_H 5.32 assigned as the 16-H proton could not be fully analysed due to overlap with another signal. However, the chemical shift of the protons on C-18 had not changed relative to the parent oxime: this is consistent with the same relative stereochemistry in both compounds *i.e.* β-acetoxy.[29] Whereas the steric strain in the lactam ring will be relieved due to resonance and whereas an acetoxy group for mechanistic reasons cannot epimerise thermally as, for example, a bromide α to a carbonyl group, the assignment nonetheless remains uncertain. For this reason, we decided to investigate the corresponding oxime without the 16-acetoxy functionality. Although we were not able to determine the configuration of **14** unequivocally, the experiment was not superfluous. We are able to conclude that the Beckmann rearrangement occurred and again with retention of configuration of the group *anti* to the oxime hydroxy group. Conversely, we can conclude that the (*Z*)-oxime **13a** does not undergo isomerisation to the (*E*)-oxime under these conditions.

The more polar (*E*)-oxime **13b**, was also treated with toluene-*p*-sulfonyl chloride in pyridine for 12 days. A complex mixture of products, none of which predominated, was formed. Whereas the 16β-acetoxy group *anti* to the 17-oxime functionality could be expected to result in the formation of a Beckmann fragmentation product (a 16,17-seco-nitrile),[30] no nitrile functionality was detectable in the product mixture. None of the products were identified.

Due to the latter problems that probably originated with the 16β-acetoxy group, it was decided to investigate the 16-deoxy analogue, **5**. The 17-ketone **5** was synthesised according to the procedure of Murphy and co-workers[23,24] from the 17-oxotriacetate, **4**. Treatment of ketone **5** with hydroxylamine hydrochloride and potassium acetate in methanol at 20 °C for one day resulted in the exclusive formation of the (*E*)-oxime, **15**. In order to avoid isomerisation, oxime **15** was not recrystallised.[22] The structure of **15** was assigned on the basis of the chemical shift and multiplicity of the 16β-H proton. This 16β-H was observed as a quintet at δ_H 2.60 ppm. The deshielding was due to the anisotropy of the (*E*)-oxime group.[14a,b]

This (*E*)-oxime **15** was treated for 24 h with toluene-*p*-sulfonyl chloride in pyridine. Only one product was isolated. It was readily assigned as a lactam on the basis of IR and ^{13}C NMR spectroscopy. The one proton triplet at δ_H 3.26 (*J* 2.8 Hz) in the ^1H NMR spectrum was assigned as the 13-H proton with a β-configuration. The Beckmann rearrangement product was therefore assigned the structure **16**. Thus both of these oximes derived from the C-17 ketones undergo the normal Beckmann rearrangement, namely migration of the *anti*-group, with retention of configuration.

In summary, the course of the Beckmann rearrangement of rings A, C and D ketoximes of the 9β steroids followed the pathway that 9α steroids and triterpenes[6–9] undergo. That is, migration of that group *anti* to the oxime hydroxy occurred and with retention of configuration of that group.[6–9,10] The ring C, 11(*E*)-ketoxime **6**, was the substrate of main focus since the oxime functional group adjoined the 9β centre. The latter stereocentre has a dominating effect on the steroid nucleus, for example it engenders sufficient strain to drive, both *in vivo* and *in vitro*, the protosterol fusidic acid to lanosterol *via* a deep-seated backbone rearrangement.[31] However, this strain did not induce an anomalous Beckmann rearrangement. The Beckmann rearrangement of the 11(*E*)-ketoxime resulted in the 9β C-homolactam, **7**. This paralleled exactly the 9α-series. In the case of the latter, 9α-C-homolactams are observed.[9] Additionally, we have been able to establish that when mixtures of lactams were detected as in the case of the 3(*Z*)-ketoxime, **8b**, that this effect was due to *E–Z* ketoxime interconversion prior to the Beckmann rearrrangement step.

Experimental

Melting points were determined on a Thomas Hoover Capillary melting point apparatus and are uncorrected. IR spectra were recorded as KBr discs (solids) on Mattson Polaris FTIR or Perkin-Elmer 682 spectrophotometers. Optical rotations were recorded for solutions in chloroform at ambient temperature with a Perkin-Elmer 141 polarimeter. ^1H and ^{13}C NMR spectra were obtained for solutions in $CDCl_3$ with tetramethylsilane (TMS) as internal standard using a JEOL GSX spectrometer at 270 and 67.8 MHz respectively at University College, Cork unless otherwise stated. Chemical shifts, δ, are expressed in parts per million, positive shifts being downfield from TMS. Splitting patterns in ^1H NMR spectra are designated as s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; and m, multiplet. Coupling constants *J*, are in Hertz. The ^{13}C chemical shifts were assigned to C, CH, CH_2 and CH_3 by using ^{13}C

DEPT experiments with $\theta = 90$ and 135°. The mass spectra and ^{1}H NMR spectra at 400 MHz were recorded at the University of Birmingham, UK. Elemental analyses were performed at the Microanalytical Laboratory, University College Cork. Pyridine was dried by heating it at reflux temperature over potassium hydroxide pellets under N_2 for some hours and then distilling from KOH under N_2. Silica gel 60 of partical size 0.04–0.063 μm (230–400 mesh ASTM) (Arb. 7747) was used for flash column chromatography. The diameter of the column used for flash chromatography was about 1.5 inches. Aluminium sheets coated with silica gel 60 F_{254} of 0.2 mm thickness (DC-Alufolien, Merck) were used for thin layer chromatography (TLC). Silica gel 60 PF_{254} was used in preparative thick layer chromatography (PLC). Cerium(III) solution was used as a visualising reagent. In this case, the plates were sprayed with this reagent and then heated. The constituents of this cerium(III) solution were water (994 ml), phosphomolybdic acid (25 g), ceric sulfate (10 g) and concentrated sulfuric acid (60 ml). Specific rotations in g ml^{-1} were measured in chloroform.

Methyl 3-oxo-24,25-dihydrofusidate 3

Mp 106.5–108 °C (diethyl ether–heptane) (Found: C, 72.3; H, 9.3. $C_{32}H_{50}O_6$ requires C, 72.4; H, 9.5%); $[\alpha]_D$ +21.2 (*c* 0.1482); ν_{max}/cm^{-1} 3600, 1720 and 1710; δ_H 0.84 (6H, d, *J* 6, 26-, 27-H), 0.94 (3H, s, 18-H), 1.02 (3H, d, *J* 6, 30-H), 1.18 (3H, s, 19-H), 1.32 (3H, s, 32-H), 2.0 (3H, s, OAc), 3.04 (1H, d, *J* 11.4, 13-H), 3.66 (3H, s, 21-CO_2CH_3), 4.40 (1H, m, 11-H) and 5.86 (1H, d, *J* 8.5, 16-H); δ_C 12.3 (CH_3), 17.9 (CH_3), 21.1 (CH_3), 21.9 (CH_2), 22.5 (CH_3), 22.6 (CH_3), 24.7 (CH_3), 27.6 (CH), 27.8 (CH_2), 28.2 (CH_3), 29.0 (CH_2), 33.5 (CH_2), 35.4 (CH_2), 36.0 (CH_2), 36.9 (C), 38.1 (CH_2), 38.6 (CH_2), 39.0 (CH_2), 39.4 (C), 43.7 (CH), 45.4 (CH), 45.7 (CH), 48.3 (C), 48.7 (CH), 51.5 (CH_3), 68.1 (CH), 74.3 (CH), 131.2 (C), 147.3 (C), 170.4 (C), 170.8 (C) and 213.7 (C).

Methyl 3-*O*-acetyl-11(*E*)-hydroxyimino-24,25-dihydrofusidate 6

Mp 96–99 °C (methanol–water) (Found: C, 69.1; H, 9.2; N, 2.2. $C_{34}H_{53}NO_7$ requires C, 69.5; H, 9.1; N, 2.4%); $[\alpha]_D$ +17.9 (*c* 0.1249); δ_H 0.82 (3H, d, *J* 6, 30-H), 0.86 (6H, d, *J* 6, 26-, 27-H), 1.04 (3H, s, 18-H), 1.10 (3H, s), 1.12 (3H, s), 2.0, (3H, s, OAc), 2.08 (3H, s, OAc), 2.41 (1H, m), 2.64 (2H, m, one of which is 13α-H), 3.67 (3H, s, 21-CO_2CH_3), 3.94 (1H, dd, *J* 13.9 and *J* 4.7, 12α-H), 4.94 (1H, m, 3-H) and 5.84 (1H, d, *J* 8.1, 16-H); δ_C 15.7 (CH_3), 16.9 (CH_3), 20.4 (CH_2), 21.0 (CH_3), 21.3 (CH_3), 21.6 (CH_3), 21.7 (CH_3), 22.5 (CH_3), 22.6 (CH_3), 25.9 (CH_2), 27.3 (CH_2), 27.5 (CH_2), 27.8 (CH), 29.2 (CH_2), 29.7 (CH_2), 31.7 (CH_2), 34.3 (CH), 37.7 (C), 38.4 (CH_2), 38.5 (CH_2), 39.6 (CH), 40.7 (C), 46.3 (CH), 48.7 (C), 51.2 (CH), 51.5 (CH_3), 74.2 (CH), 74.5 (CH), 131.5 (C), 145.8 (C), 158.8 (C), 170.4 (C), 170.5 (C) and 171.2 (C).

Methyl 3-*O*-acetyl-11-aza-11a-homo-11a-oxo-24,25-dihydrofusidate 7

Tosyl chloride (1.22 g, 6.4 mmol) was added to a solution of (*E*)-11-oxime **6** (1.22 g, 2.08 mmol) in dry pyridine. The solution was left at 20 °C under a nitrogen atmosphere for 306 h. After work-up, the silica gel TLC indicated a faint less-polar spot which corresponded to the starting oxime and an intense more-polar spot of the product **7**. The crude product (0.83 g) was purified by dry flash column chromatography on silica gel using a gradient elution of ethyl acetate and dichloromethane (2:1) on a 3 cm diameter column. The weight of the purified *product* **7** was 0.673 g (81%), mp 214–215 °C (diethyl ether–heptane) (Found: C, 69.6; H, 9.1; N, 2.2. $C_{34}H_{53}NO_7$ requires C, 69.5; H, 9.1; N, 2.4%); $[\alpha]_D$ +8.2 (*c* 0.135); ν_{max}/cm^{-1} 3320, 1700 and 1635; δ_H 0.82 (3H, d, 30-H), 0.88 (6H, d, *J* 6, 26-, 27-H), 1.03 (3H, s, 18-H), 1.12 (3H, s), 1.14 (3H, s), 2.01 (3H, s, OAc), 2.10 (3H, s, OAc), 2.42 (2H, m), 2.80 (2H, q, 12-H), 3.0 (1H, d, *J* 11.3, 13α-H), 3.6 (1H, d, 9-H), 3.66 (3H, s, 21-CO_2CH_3), 4.92 (1H, m, 3-H), 5.74 (1H, d, *J* 8.5, 16-H) and 5.88 (1H, d, N-H); δ_C 15.0 (CH_3), 17.6 (CH_3), 18.0 (CH_3), 21.0 (CH_3), 21.3 (CH_3), 21.8 (CH_2), 22.5 (CH_3), 23.0 (CH_3), 25.2 (CH_2), 26.2 (CH_2), 27.5 (CH_2), 27.7 (CH), 29.4 (CH_2), 30.4 (CH_2), 34.3 (CH), 34.3 (CH_2), 36.2 (CH), 37.6 (CH_2), 38.5 (CH_2), 39.8 (C), 42.9 (C), 45.4 (CH), 49.3 (C), 51.6 (CH_3), 57.9 (CH), 72.5 (CH), 73.0 (CH), 133.2 (C), 144.7 (C), 170.2 (C), 170.5 (C), 170.7 (C) and 174.4 (C); M^+ 587.3822. $C_{34}H_{53}NO_7$ requires 587.7952.

Methyl 3(*E*)-hydroxyimino-24,25-dihydrofusidate 8a

Mp 144.5–145.5 °C (diethyl ether–hexane) (Found: C, 70.7; H, 10.0; N, 2.6. $C_{32}H_{51}NO_6$ requires C, 70.3; H, 9.6; N, 2.6%); $[\alpha]_D$ −9.81 (*c* 0.1247); ν_{max}/cm^{-1} 3570, 3350, 1750, 1650 (weak) and 900; δ_H 0.86 (3H, d, *J* 6, 27-H), 0.86 (3H, d, *J* 6, 26-H), 0.94 (3H, s, 18-H), 1.08 (3H, s, 19-H), 1.10 (3H, d, 30-H), 1.32 (3H, s, 32-H), 2.0 (3H, s, OAc), 3.02 (1H, d, *J* 11.4 , 13α-H), 3.24 (1H, m, 2α-H), 3.66 (3H, s, 21-CO_2CH_3), 4.38 (1H, m, 11-H) and 5.84 (1H, d, *J* 8.5, 16-H); δ_C 13.9 (CH_3), 17.8 (CH_3), 20.6 (CH_2), 21.0 (CH_3), 21.6 (CH_2), 22.6 (CH_3), 22.7 (CH_3), 24.0 (CH_3), 27.2 (CH), 27.6 (CH_3), 27.8 (CH_2), 29.0 (CH_2), 33.2 (CH_2), 34.3 (CH_2), 36.0 (CH_2), 36.9 (CH), 37.3 (C), 38.4 (CH_2), 38.6 (C), 39.0 (CH_2), 43.7 (CH), 45.1 (CH), 48.7 (CH), 48.9 (C), 51.6 (CO_2CH_3), 68.1 (CH), 74.3 (CH), 131.1 (C), 147.3 (C), 162. 8 (C), 170.5 (C) and 170.9 (C).

Methyl 3(*Z*)-hydroxyimino-24,25-dihydrofusidate 8b

(Found: C, 70.5; H, 9.9; N, 2.6. $C_{32}H_{51}NO_6$ requires C, 70.3; H, 9.6; N, 2.6%); ν_{max}/cm^{-1} 3500, 1750, 1730 and 1650 (weak); δ_H 0.86 (3H, s, 18-H), 0.86 (6H, d, *J* 6, 26-, 27-H), 0.94 (3H, s, 19-H), 1.12 (3H, d, *J* 6, 30-H), 1.36 (3H, s, 32-H), 2.0 (3H, s, OAc), 2.68 (2H, m, one of which is 4β-H), 3.02 (1H, d, *J* 11.4, 13α-H), 3.66 (3H, s, 21-CO_2CH_3), 4.38 (1H, m, 11-H) and 5.86 (1H, d, *J* 8.5, 16-H); δ_C 14.5, 18.3, 21.1, 22.6, 24.0, 24.5, 25.7, 27.6, 27.8, 29.1, 32.3, 33.2, 35.5, 36.0, 36.6, 38.6, 39.1, 39.4, 43.7, 43.9, 46.7, 48.9, 51.5, 68.0, 74.3, 131.3, 147.8, 166.0, 170.5 and 170.8.

Methyl 3a-aza-3a-homo-3-oxo-24,25-dihydrofusidate 9

Tosyl chloride (0.382 g, 2.004 mmol, 2.3 molar equivalents) was added to a solution of methyl 3(*E*)-hydroxyimino-24,25-dihydrofusidate **8a** (0.48 g, 0.88 mmol) in dry pyridine. The solution was permitted to stand at 20 °C under a N_2 atmosphere for 102 h. After work-up the crude product (0.49 g) was washed through a one inch column of silica gel with ethyl acetate. The weight of the crude product was 0.38 g after washing. Purification of the crude product by flash chromatography on silica gel (60 g) using 1:3 hexane–ethyl acetate and then 100% ethyl acetate as eluents, yielded 0.24 g (62.5%) of the *product* **9**, mp 168.5–170 °C (ethanol–heptane) (Found: C, 70.4; H, 9.5; N, 2.4. $C_{32}H_{51}NO_6$ requires C, 70.3; H, 9.6; N, 2.6%); $[\alpha]_D$ +26.18 (*c* 0.0912); ν_{max}/cm^{-1} 3400, 1735 and 1650; δ_H 0.85 (6H, d, *J* 6, 26-, 27-H), 0.92 (3H, s, 32-H), 1.12 (3H, s, 19-H), 1.20 (3H, d, *J* 6.2, 4aα-CH_3), 1.30 (3H, s, 32-H), 2.0 (3H, s, OAc), 3.03 (1H, d, *J* 11.4, 13α-H), 3.40 (1H, m, 4aβ-H), 3.65 (3H, s, 21-CO_2CH_3), 4.40 (1H, m, 11-H), 5.85 (1H, d, *J* 8.5, 16-H) and 6.0 (1H, d, N-H); δ_C 18.0 (CH_3), 20.8 (CH_3), 21.0 (CH_3), 22.5 (CH_2), 22.6 (CH_3), 22.6 (CH_3), 22.8 (CH_3), 25.6 (CH_3), 27.6 (CH_2), 27.8 (CH), 29.0 (CH_2), 32.4 (CH_2), 33.4 (CH_2), 35.4 (CH_2), 36.3 (CH_2), 38.6 (CH_2), 39.07 (C), 39.1 (CH_2), 39.4 (C), 43.9 (CH), 47.6 (CH), 48.4 (CH), 48.7 (CH), 48.9 (C), 51.4 (CH_3), 67.4 (CH), 74.3 (CH), 131.4 (C), 148.1 (C), 171.0 (C), 171.1 (C) and 177.0 (C).

Beckmann rearrangement of methyl 3(*Z*)-hydroxyimino-24,25-dihydrofusidate 8b

Tosyl chloride (0.041 g, 0.22 mmol, 2.3 molar equivalents) was added to a solution of methyl 3(*Z*)-hydroxyimino-24,25-

dihydrofusidate **8b** (0.051 g, 0.093 mmol) in dry pyridine. The solution was kept at 20 °C under a nitrogen atmosphere for 102 h. After work-up, purification of the crude product (48 mg) by silica gel PLC using 1 : 3 hexane–ethyl acetate as eluent with two elutions gave the product (29.2 mg, 57.3%), which was a mixture of two lactams **9** and **10** (Found: C, 70.3; H, 9.4; N, 2.7. $C_{32}H_{52}NO_6$ requires C, 70.3; H, 9.6; N, 2.6%); δ_H 0.85 (d, *J* 6, 26-, 27-H of both lactams **9** and **10**), 0.92 (s, 18-H of **9**), 0.94 (s, 18-H of **9**), 1.12 (s, 19-H of **10**), 1.20 (d, *J* 6.2, 4aα-CH_3), 1.26 (s, 19-H of **10**), 1.30 (s, 32-H of **9**), 1.32 (s, 32-H of **10**), 2.0 (s, OAc of both lactams **9** and **10**), 3.03 (d, *J* 11.4, 13α-H of both lactams **9** and **10**), 3.22 (d m, 2α-H of **10**), 3.40 (m, 4aβ-H of **9**), 3.64 (s, 21-CO_2CH_3 of both lactams **9** and **10**), 4.40 (m, 11-H of **9**), 4.44 (m, 11-H of **10**) and 5.85 (d, *J* 8.5, 16-H of both lactams **9** and **10**). The ratio of isomers was determined by comparing the relative integrations of the multiplet at δ_H 3.40 with that of the doublet of multiplets at δ_H 3.22. Separation of these two lactams by silica gel TLC using a wide range of different eluents, failed.

Lactone 12

Mp 197–198.5 °C (acetone–heptane) (Found: C, 63.5; H, 7.9. $C_{33}H_{48}O_{11}$ requires C, 63.9; H, 7.8%); ν_{max}/cm^{-1} 3450, 1775, 1720 and 1700; δ_H 0.81 (3H, d, *J* 6, 30-H), 0.96 (3H, s, 18-H), 1.15 (3H, s, 19-H), 1.40 (3H, s, 32-H), 2.06, 2.02, 2.01 (9H, 3 × s, 3 × OAc), 3.84 (3H, s, 21-CO_2CH_3), 4.91 (1H, m, 3-H), 5.19 (1H, m, 11-H) and 5.20 (1H, d, *J* 8.5, 16-H); δ_C 15.6 (CH_3), 17.7 (CH_3), 20.5 (CH_2), 21.0 (CH_3), 21.3 (CH_3), 21.8 (CH_3), 22.0 (CH_3), 23.5 (CH_3), 27.2 (CH_2), 28.7 (CH_2), 29.7 (CH_2), 30.0 (CH_2), 32.8 (CH_2), 34.4 (CH), 37.0 (C), 37.8 (CH_2), 38.1 (CH), 41.4 (C), 47.8 (CH), 51.3 (CH), 51.8 (C), 53.9 (CH_3), 71.2 (CH), 74.2 (CH), 84.2 (CH), 85.2 (C-17), 85.4 (C-20), 169.4 (C), 170.3 (C), 170.8 (C), 175.0 (C) and 176.2 (C-24).

17(*Z*)-Oxime 13a

Mp 214–215 °C (acetone–heptane) (Found: C, 65.5; H, 8.5; N, 2.8. $C_{27}H_{41}NO_7$ requires C, 66.0; H, 8.4; N, 2.9%); $[\alpha]_D$ − 14.8 (*c* 0.1187); ν_{max}/cm^{-1} 3500, 1735 and 1710; δ_H 0.84 (3H, d, *J* 6, 30-H), 0.99 (3H, s, 18-H), 1.03 (3H, s, 19-H), 1.43 (3H, s, 32-H), 2.02 (3H, s, OAc), 2.06 (3H, s, OAc), 2.07 (3H, s, OAc), 2.78 (1H, dd, *J* 2.8 and *J* 11.4, 13α-H), 4.94 (1H, m, 3-H), 5.3 (1H, m, 11-H) and 5.96 (1H, d, *J* 8.5, 16-H); δ_C 15.6 (CH_3), 17.4 (CH_3), 20.4 (CH_2), 21.2 (CH_3), 21.3 (CH_3), 21.8 (CH_3), 22.3 (CH_3), 23.6 (CH_3), 27.3 (CH_2), 28.8 (CH_2), 29.6 (CH_2), 32.5 (CH_2), 34.6 (CH), 37.1 (CH), 37.9 (CH_2), 38.9 (C), 39.9 (C), 42.5 (CH), 48.3 (C), 48.7 (CH), 68.5 (CH), 70.2 (CH), 74.1 (CH), 162.1 (C), 170.1 (C), 170.2 (C) and 170. 8 (C).

17(*E*)-Oxime 13b

Mp 215–216 °C (acetone–heptane) (Found: C, 65.5; H, 8.6; N, 2.6. $C_{27}H_{41}NO_7$ requires C, 65.96; H, 8.4; N, 2.9%); $[\alpha]_D$ −25.7 (*c* 0.1655); ν_{max}/cm^{-1} 3450, 1730 and 1710; δ_H 0.82 (3H, d, *J* 6, 30-H), 1.0 (3H, s, 18-H), 1.06 (3H, s, 19-H), 1.39 (3H, s, 32-H), 2.03, 2.04, 2.05 (9H, 3 × s, 3 × OAc), 2.26 (1H, dd), 2.78 (1H, dt, *J* 14.65, 3, 12α-H), 2.84 (1H, dd, *J* 12.98, 3, 13-H), 4.94 (1H, br s, 3-H), 5.26 (1H, br s, 11-H) and 5.52 (1H, d, *J* 8.5, 16-H); δ_C 15.6 (CH_3), 18.7 (CH_3), 20.3 (CH_2), 21.2 (CH_3), 21.3 (CH_3), 21.9 (CH_3), 22.3 (CH_3), 23.8 (CH_3), 27.3 (CH_2), 29.7 (CH_2), 31.2 (CH_2), 32.4 (CH_2), 34.6 (CH), 36.9 (CH), 37.7 (CH_2), 38.2 (C), 39.7 (C), 44.1 (CH), 48.1 (CH), 48.4 (C), 70.6 (CH), 71.8 (CH), 74.1 (CH), 160.7 (C), 170.2 (C), 170.6 (C) and 170.8 (C).

(3α,4α,5α,8α,9β,11α,13α,14β,16β)-3,11,16-Triacetoxy-4,8,14-trimethyl-17a-aza-17a-homo-18-norandrostan-17-one 14

The (*Z*)-oxime **13a** (0.605 g, 1.23 mmol) was dissolved in dry pyridine. Tosyl chloride (0.706 g, 3.7 mmol) was added. The solution was left under a N_2 atmosphere at 20 °C for 12 days. After work-up, the weight of the crude product was 0.6 g. Purification of the crude product (0.41 g) by flash chromatography on silica gel (60 g) using 1 : 4 dichloromethane–ethyl acetate as eluent gave the *product* **14** (0.185 g, 45%), mp 269 °C (acetone–heptane) (Found: C, 65.7; H, 8.5; N, 3.0. $C_{27}H_{41}NO_7$ requires C, 65.96; H, 8.4; N, 2.9%); $[\alpha]_D$ −23.9 (*c* 0.0174); ν_{max}/cm^{-1} 3330, 1715, 1725 and 1690; δ_H 8.2 (3H, d, *J* 6, 30-H), 1.0 (6H, s, 19-, 18-H), 1.48 (3H, s, 32-H), 2.02 (6H, s, 2 × OAc), 2.18 (3H, s, OAc), 2.48 (1H, dd, *J* 9 and *J* 15.4), 3.84 (1H, dd, *J* 11.8 and *J* 4.7), 4.94 (1H, m, 3-H), 5.30 (1H, m, 11-H), 5.32 (1H, probably dd, 16-H) and 6.04 (1H, m, N-H); δ_C 15.5 (CH_3), 16.9 (CH_3), 20.7 (CH_2), 21.0 (CH_3), 21.2 (CH_3), 21.7 (CH_3), 23.0 (CH_3), 23.3 (CH_3), 27.1 (CH_2), 29.5 (CH_2), 31.4 (CH_2), 32.7 (CH_2), 35.1 (CH), 35.3 (CH_2), 37.0 (C), 37.5 (CH), 40.6 (C), 43.0 (C), 48.5 (CH), 49.0 (CH), 67.7 (CH), 69.7 (CH), 73.9 (CH), 169.5 (C), 170.1 (C), 170.2 (C) and 170.6 (C).

(3α,4α,5α,8α,9β,13β,14β,17*E*)-3-Acetoxy-4,8,14-trimethyl-18-norandrostan-17-one oxime 15

(Found: C, 73.5; H, 9.9; N, 4.0. $C_{23}H_{37}NO_3$ requires C, 73.6; H, 9.9; N, 3.7%); $[\alpha]_D$ −15.3 (*c* 0.0563); ν_{max}/cm^{-1} 3445, 3420 and 1700; δ_H 0.80 (3H, d, *J* 6, 30-H), 0.92 (3H, s, 18-H), 1.02 (3H, s, 19-H), 1.20 (3H, s, 32-H), 2.04 (3H, s, OAc), 2.60 (1H, quintet, 16-H) and 4.92 (1H, m, 3-H); δ_C 15.4 (CH_3), 19.8 (CH_2), 21.1 (CH_2), 21.3 (CH_3), 21.9 (CH_3), 22.2 (CH_2), 23.7(CH_3), 25.8 (CH_3), 26.8 (CH_2), 26.9 (CH_2), 30.0 (CH_2), 32.5 (CH_2), 32.8 (CH_2), 35.2 (CH), 37.7 (C), 38.5 (CH), 40.0 (C), 48.8 (CH), 49.1 (C), 50.3 (CH), 74.6 (CH), 169.4 (C) and 171.4 (C).

(3α,4α,5α,8α,9β,13β,14β)-3-Acetoxy-4,8,14-trimethyl-17a-aza-17a-homo-18-norandrostan-17-one 16

Tosyl chloride (0.68 g, 3.6 mmol, 3 molar equivalents) was added to a solution of 3-acetoxy-4,8,14-trimethyl-18-norandrostan-17-one oxime **15** (0.45 g, 1.2 mmol) in dry pyridine. The solution was left under a nitrogen atmosphere for 24 h at 20 °C. After work-up, purification of the crude product (0.44 g) by flash chromatography on silica gel (60 g) using 1 : 1 dichloromethane–ethyl acetate and then 100% ethyl acetate as eluents gave the *product* **16** (0.30 g, 67%), mp 158–160 °C (acetone–heptane) (Found: C, 72.0; H, 10.0, N, 3.7. $C_{23}H_{37}NO_3 \cdot 1/2H_2O$ requires C, 71.8; H, 9.7; H, 3.6%); $[\alpha]_D$ −57.0 (*c* 0.052); ν_{max}/cm^{-1} 3165, 3040, 1725 and 1660; δ_H 0.82 (3H, d, *J* 6, 30-H), 0.94 (3H, s, 18-H), 1.06 (3H, s, 19-H), 1.24 (3H, s, 32-H), 2.06 (3H, s, OAc), 2.34 (2H, dd, *J* 5.7 and *J* 7.8), 3.26 (1H, t, *J* 2.8, 13β-H) and 4.92 (1H, m, 3-H); δ_C 15.4 (CH_3), 19.1 (CH_2), 20.8 (CH_2), 21.3 (CH_3), 22.0 (CH_3), 23.4 (CH_3), 24.3 (CH_3), 26.9 (CH_2), 27.0 (CH_2), 27.8 (CH_2), 28.3 (CH_2), 30.0 (CH_2), 31.9 (CH_2), 34.9 (CH), 36.0 (C), 37.5 (CH), 40.0 (C), 40.6 (C), 45.1 (CH), 56.9 (CH), 74.3 (CH), 170.9 (C) and 174.6 (C).

X-Ray analysis of methyl 3-*O*-acetyl-11-aza-11a-homo-11a-oxo-24,25-dihydrofusidate 7

Selected bond lengths are given in Table 1, and details of the cell data, data collections and refinement for **7** are summarised in Table 2. Molecule **7** crystallised in the monoclinic system; space group $P2_1$ from the systematic absences and the known chirality of the sample. The structure was solved using SHELXS-97[32] and refinement was by full-matrix least-squares calculations on F^2 with all measured data using SHELXL-97.[33] The carbonyl O and O-Me groups of the ester function had very prolate distribution of their anisotropic displacement parameters at an early stage of the refinement. In the final rounds of calculations the carbonyl O and O-Me groups were allowed for as disordered models with two equal occupancies, namely, the almost planar components [C21(=O21A)–O21B–C21B] and [C21(=O21C)–O21D–C21D]. The interplanar angle between these groups of atoms is 37 degrees. H atoms were visible in difference maps and were treated as riding atoms (C–H 0.96 to 0.98, N–H 0.86 Å). The H atoms of the acetyl

Table 1 Selected bond lengths, involving the oxygen and nitrogen atoms

Bond	Distance/Å	Bond	Distance/Å
O(1)–C(1A)	1.295(16)	O(1)–C(3)	1.482(15)
O(2)–C(1A)	1.195(18)	O(3)–C(11)	1.230(19)
O(4)–C(4A)	1.350(18)	O(4)–C(16)	1.446(17)
O(5)–C(4A)	1.188(18)	O(6)–C(21)	1.170(22)
O(7)–C(21)	1.246(19)	O(7)–C(28)	1.455(17)
N–C(9)	1.464(18)	N–C(11)	1.340(16)
C(17)–C(20)	1.338(18)		

Table 2 Summary of crystal data, data collection, structure solution and refinement details for **7**

(a) Crystal data	
Empirical formula	$C_{34}H_{53}NO_7$
Molar mass	587.77
Color, habit	colorless, plate
Crystal size, mm	0.35 × 0.20 × 0.07
Crystal system	monoclinic
a/Å	9.5343(9)
b/Å	12.655(4)
c/Å	13.9326(17)
α (°)	90
β (°)	94.862(10)
γ (°)	90
V/Å^3	1675.0(6)
Space group	$P2_1$
Z	2
F(000)	640
d_{calc}/g cm^{-3}	1.165
μ/mm^{-1}	0.080
(b) Data acquisition[a]	
Temp./K	294(1)
Unit-cell reflcns [*θ*-range (°)]	9.0 (13.0)
Max. *θ* (°) for reflcns	24.90
hkl range of reflcns	−11 11; 0 13; 0 16
Variation in 3 standard reflcns	1.0%
Reflcns measured	3050
Unique reflcns	2932
R_{int}	0.012
Reflcns with $I > 2\sigma(I)$	1312
(c) Structure solution and refinement[b]	
Refinement on	F^2
Solution method	direct methods
H-atom treatment	riding
No. of variables in L.S.	389
Weights: *k* in $w = 1/(\sigma^2F_o^2 + k)$	$(0.0570P)^2$ $[P = (F_o^2 + 2F_c^2)/3]$
R, R_w, *gof*	0.055, 0.110, 0.90
Density range in final Δ map/e Å^{-3}	−0.156, 0.163
Final shift/error ratio	0.000
Sec. extnct. type	SHELXL
Sec. extnct. correction	0.0063(16)

[a] Data collection on an Enraf–Nonius CAD4 diffractometer with graphite monochromatised Mo-Kα radiation (λ 0.710 Å). [b] All calculations were done on a Silicon Graphics 4D-35TG computer system with the NRCVAX programs.[36]

methyl groups and of the methyl ester groups were disordered and this was allowed for using the AFIX-123 command in SHELX-97.

In the refinement cycles, all non-H atoms were allowed anisotropic displacement parameters. The ORTEP[34] plot was made with the aid of PLUTON.[35]

The absolute configuration of the parent fusidic acid has been established previously by an X-ray analysis of a *p*-bromobenzoate derivative[1c] and the same configuration was chosen for the refinement of **7.** Although there are no significant anomalous scattering atoms in **7** we used the NRCVAX programme BIJVOET[36] to calculate which reflections would have the largest (but still small) Bijvoet differences; careful re-measurement of the thirteen reflections which gave the largest differences were in accord with the absolute configuration established previously.[1c]

The final positional and displacement parameters and a full list of dimensions involving all non-H atoms have been deposited with the Cambridge Crystallographic Data Centre (CCDC) and are also available from the authors in CIF format. For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc.*, *Perkin Trans. 1*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/276.

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