Pergamon

Tetrahedron Vol. 50, No. 36, pp. 10783-10790, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4020/94 \$7.00+0.00

0040-4020(94)00651-2

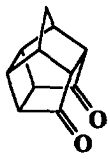
Synthesis of δ-Lactams from Pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]Undecane-8,11-Dione

Frans J.C. Martins[a]*, Agatha M. Viljoen[a]*, Hendrik G. Kruger[a], Johan A. Joubert[a] and Philippus L. Wessels[b]

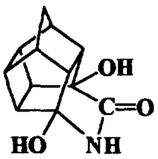
[a]Department of Chemistry, Potchefstroom University for C.H.E., Potchefstroom 2520, South Africa
[b]Department of Chemistry, University of Pretoria, Pretoria 0001, South Africa

Abstract: *The influence of reaction conditions on the conversion of pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-dione to lactam derivatives was investigated. Treatment with one equivalent aqueous sodium cyanide produced 8,11-dihydroxy-pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-lactam. With two equivalents aqueous sodium cyanide 11-cyano-8-hydroxy-pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-lactam was obtained. Treatment with an aqueous mixture of sodium cyanide, ammonium chloride and ammonia produced 11-amino-8-hydroxy-pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-lactam. In acidic media 11-cyano-8-hydroxy-pentacylo-[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-lactam was converted to the 11-cyano, 11-amido or 11-carboxylic acid 8,11-lactone derivatives respectively depending on the applied reaction conditions.*

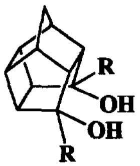
It has recently been reported[1] that pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-dione (**1**) produces the dihydroxy lactam derivative **2** upon treatment with one equivalent aqueous sodium cyanide. As part of a program designed to explore the synthesis and chemistry of amino acids and lactams containing polycyclic cage moieties, we have examined the influence of reaction conditions on the conversion of **1** to lactam derivatives utilising Strecker reagents.



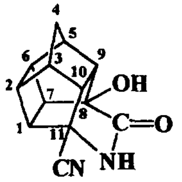
1



2



3, R = H
4, R = CH_3
5, R = CN



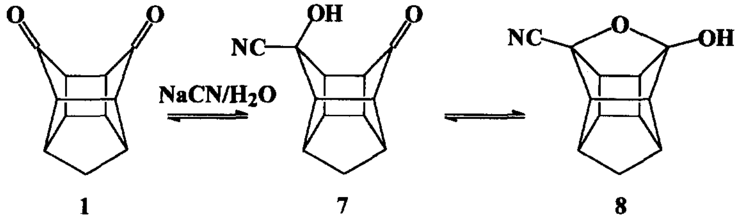
6

It is expected that treatment of **1** with two equivalents or more aqueous sodium cyanide should force both carbonyl groups to suffer nucleophilic attack from cyanide anions whereby the formation of **2** should be inhibited. Nucleophilic attack on the carbonyl carbon atoms of **1** is expected to take place on the *exo* face of the carbonyl groups as a result of the proximity of the groups. For example, it was previously shown that treatment of **1** with lithium aluminium hydride and methyl magnesium iodide respectively affords **3**[2] and **4**[3]. It is therefore anticipated that treatment of **1** with two equivalents or more sodium cyanide should produce **5**. Surprisingly the reaction took a different course and afforded the lactam **6**.

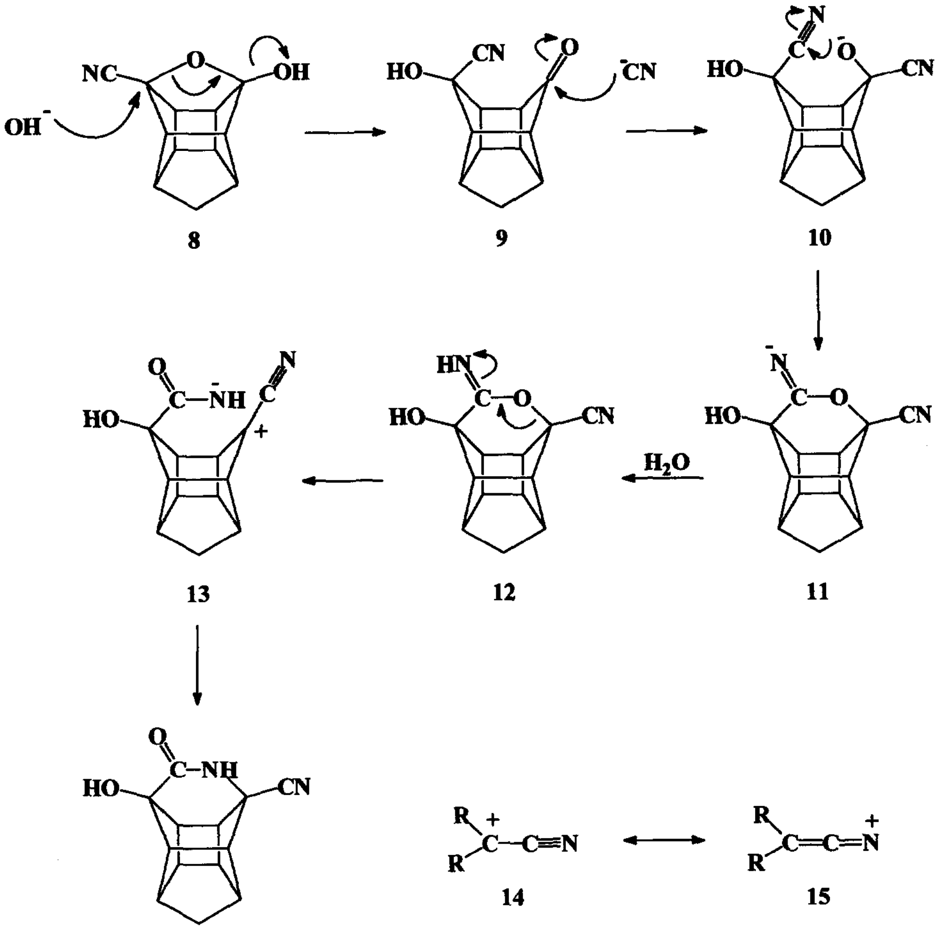
The electron impact induced (EI) mass spectrum of **6** exhibits a weak molecular ion at m/z 228. A fast atom bombardment (FAB) mass spectrometrical analysis with a glycerol matrix containing hydrochloric acid shows a strong pseudo molecular ion peak at m/z 229 [$(M+H)^+$]. An elemental analysis supported a molecular formula of $C_{13}H_{12}N_2O_2$. The infrared spectrum of **6** displays a N-H stretching vibration absorption peak at 3 435 cm^{-1}, an O-H stretching vibration absorption at 3 295 cm^{-1}, a weak C-N triple-bond stretching vibration absorption at 2 245 cm^{-1} and a strong carbonyl group absorption at 1 680 cm^{-1}. These data are supportive of the proposed structure of **6**. Confirmative evidence for the correctness of the allocated structure of **6** was obtained from a ^1H and ^{13}C n.m.r. study.

The 300 MHz ^1H n.m.r. spectrum [$(CD_3)_2SO$] of **6** shows signals of an AB spin system for the methylene protons and a complex pattern of resonance signals between δ_H 2.35 and δ_H 3.25 integrating for eight protons. Two singlets are registered at δ_H 6.06 and δ_H 7.95 which disappeared on treatment with D_2O and are respectively attributable to a hydroxyl group proton and a proton coupled to a nitrogen atom. The ^{13}C n.m.r. spectrum of **6** exhibits signals for thirteen different carbon atoms. The resonance at δ_C 118.23 can be assigned to a nitrile carbon atom. Two quaternary carbon atom resonances are registered at δ_C 77.27 and δ_C 76.43 and a carbonyl carbon resonance appears at δ_C 171.50. The methylene carbon atom resonance is registered at δ_C 36.25. The ^{13}C n.m.r. spectrum of **6** also exhibits signals of eight methine carbon atoms. The positions of the NH and OH groups were established by a ^{13}C n.m.r. study of a sample in which partial exchange of protons with deuterium atoms was imposed by addition of a mixture of 60% D_2O and 40% H_2O. The quaternary carbon resonance signal at δ_C 76.43 (C-11) was registered as a double signal due to the α-isotopic effect of the NH group. The quaternary carbon resonance at δ_C 77.27 (C-8) displayed signals characteristic of α- and β-effects as was the case for the carbonyl carbon resonance at δ_C 171.50.

If it is accepted that the attack of all external reagents on the carbonyl groups of **1** will be on the *exo* face, the "inversion" of a nitrile group can only be explained if it is assumed that the cyclic ether **8** plays an intermediate role in the conversion of **1** to **6**. (The structures have been redrawn from a different viewpoint in order to emphasise the geometry of the boat cyclohexane ring which is more "buckled" than a standard boat cyclohexane). It was previously shown[1] that **7** and **8** act as intermediates in the conversion of **1** to **2**. The explanation previously given[1] for the conversion of **1** to **2** can, however, not account for the formation of a compound such as **6**.



Nucleophilic attack of hydroxide which is necessary to "invert" the cyanide group is expected to be concerted with the loss of the hydroxide group in **8** whereby **9** should be formed. With an excess cyanide ions in the reaction mixture nucleophilic attack of cyanide ions on the carbonyl carbon atom should lead to the formation of the intermediate **10** which contains *endo* and *exo* orientated cyano groups. Studies on stereo models show that the electron deficient carbon atom of the *endo* cyano group in **10** is in a favourable position to suffer attack from the nearby negatively charged oxygen atom to produce the intermediate **11** and subsequently **12**. The postulated rearrangement of **12** to the α-cyano cation **13** is not controversial since α-cyano cations of general formula **14** are significantly stabilised by charge delocalisation through resonance structures such as **15**, even though this requires a portion of the charge to reside on a divalent nitrogen.[4] The π-donor effect of cyano substituents is only manifested when attached to very unstable cations.[5] The negative charge on the nitrogen atom of **13** should also be sufficiently stabilised by the adjacent carbonyl group to promote the proposed rearrangement.

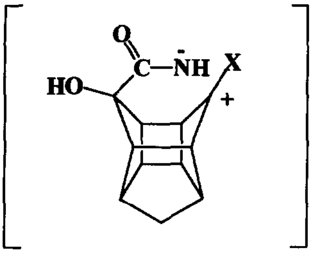


8 **9** **10**

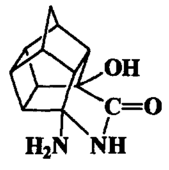
13 **12** **11**

6 **14** **15**

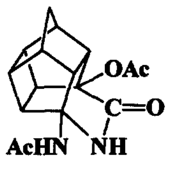
In the absence of an excess of cyanide ions attack from hydroxy anions instead of cyanide ions on the carbonyl carbon atom of **9** will explain the conversion of **1** to **2** (when **1** is treated with one equivalent of aqueous sodium cyanide). The hydroxy group in the proposed intermediate **16** (X = OH) in this case should also stabilise the positive charge on the adjacent carbon atom explaining the conversion of **1** to **2**. Similarly it should be possible by manipulation of the nucleophiles present (e.g. with an excess ammonia) to obtain a resonance stabilised intermediate such as **17** (X = NH_2) whereby **18** should be obtained.



16, X = OH
17, X = NH_2



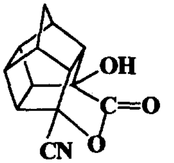
18



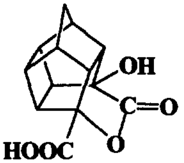
19

Treatment of **1** with an aqueous mixture of one equivalent sodium cyanide, ammonium chloride and an excess ammonium hydroxide indeed resulted in the formation of **18**. The infrared spectrum of **18** exhibits strong absorption bands in the O-H and N-H stretching vibration region at 3 380, 3 295, 3 290 and 3 165 cm^{-1}. A carbonyl group absorption is registered at 1 655 cm^{-1}. An elemental analysis is supportive of a molecular formula of $C_{12}H_{14}N_2O_2$ which was confirmed by a mass spectrum showing a molecular ion at m/z 218. The ^{13}C n.m.r. spectrum of **18** exhibits twelve signals representative of a carbonyl carbon resonance (δ_C 174.37), two quaternary carbon resonances (δ_C 80.02 and δ_C 73.71), a methylene carbon resonance (δ 36.66) and eight methine carbon resonances. The 300 MHz ^1H n.m.r. spectrum of **18** clearly shows the presence of three signals of deuterium exchangeable protons at δ_H 7.69 (NH), δ_H 4.66 (OH) and δ_H 2.54 (NH_2). A complex pattern of resonance signals is registered between δ_H 2.08 and δ_H 2.77. The methylene protons are registered as an AB spin system around δ_H 1.49. In order to gain more information on the structure of **18** acetylation was brought about by treatment with acetyl chloride. A diacetate (**19**) was obtained of which the ^1H n.m.r. spectrum shows only two deuterium exchangeable proton resonance signals at δ_H 8.24 and δ_H 8.22 typical of NH protons next to carbonyl groups. Evidence that C-11 in **19** is coupled to two deuterium exchangeable proton bearing groups was obtained from a proton noise decoupled ^{13}C n.m.r. spectrum recorded in $(CD_3)_2SO$ which was treated with two drops of a mixture of 60% D_2O and 40% H_2O to impose partial exchange to protons. As expected the quaternary carbon resonance at δ_C 73.02 is registered as three signals with the second and third signals appearing respectively 0.1 and 0.2 p.p.m. upfield. A double signal due to a β-effect of the NH group in the lactam ring is observed for the quaternary carbon atom (C-8) registered at δ_C 87.02 where the second signal appears 0.02 p.p.m. upfield. The carbonyl carbon atom resonances registered at δ_C 170.36 (CO of lactam ring) and δ_C 168.23 (CO of NH acetate) are also registered as double signals due to α-isotopic effects. (The second signals appearing respectively 0.13 and 0.17 p.p.m. upfield). The carbonyl carbon atom resonance at δ_C 168.15 is not affected by isotopic exchange.

The ability of the cyano group to stabilise an intermediate cation is clearly demonstrated by the behaviour of **6** in acidic media. Treatment of a dichloromethane solution of **6** with acetic acid produced **20** whereas treatment with hydrochloric acid afforded the carboxylic acid **21**. The latter was characterised by conversion to a hydroxy lactone mono-ester by treatment with methanol and concentrated sulphuric acid.

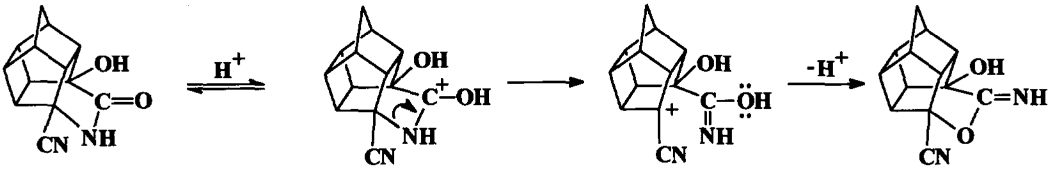


20



21

It is well known that amides and lactams are primarily protonated on the carbonyl oxygen atom. Ring cleavage of the protonated species **22** to render the mesomeric stabilised carbonium ion **23** should explain the formation of the imine **12** which should be easily hydrolysed in acidic media to the lactones **20** or **21**. The lactams **2** , **18** or **19** could not be converted to the corresponding lactones in acidic media probably due to competing protonation on the hydroxy or amino groups respectively adjacent to the expected position of ring cleavage.

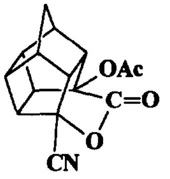


6 **22** **23** **12**

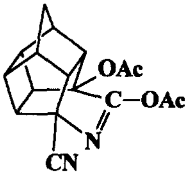
Confirmative evidence for the correctness of the structure of **20** was obtained from a ^1H and ^{13}C n.m.r. study. The 300 MHz ^1H n.m.r. spectrum $[(CD_3)_2SO]$ of **20** exhibits a complex pattern of signals between δ_H 2.50 and δ_H 3.30 integrating for eight protons, two doublets associated with an AB spin system of the methylene protons and a singlet at δ_H 5.97 which disappeared on treatment with D_2O. The ^{13}C n.m.r. spectrum shows a carbonyl carbon resonance at δ_C 172.63, a resonance at δ_C 117.39 which can be associated with a nitrile carbon atom, two quaternary carbon resonances at δ_C 79.12 and δ_C 77.45, eight methine carbon resonances and a methylene carbon resonance registered at δ_C 36.78. Evidence that C-8 is coupled to a deuterium exchangeable proton bearing group was obtained from a proton noise decoupled ^{13}C n.m.r. spectrum recorded in $(CD_3)_2SO$ which was treated with a mixture of 60% D_2O and 40% H_2O. As expected the quaternary carbon resonance at δ_C 77.45 is registered as a double signal with the second signal appearing 0.12 p.p.m. upfield. A double signal due to a β-effect is also observed for the carbonyl carbon signal at δ_C 172.63 where the second signal appears 0.03 p.p.m. upfield.

The influence of acidic conditions on the behaviour of **6** is also clearly demonstrated by derivatisation reactions carried out in acidic and non-acidic media. Acetylation of **6** with acetic anhydride and sodium acetate produced the acetate **24** which is identical to the acetate obtained from the acetylation of **20**. Acetylation of **6** with acetyl chloride in the presence of N,N-dimethylaniline to avoid acidic conditions produced the diacetate **25** indicating that the lactim tautomeric isomer is favoured under these reaction conditions. The infrared spectrum of **25** exhibits two carbonyl absorption bands at 1 765 and 1 700 cm^{-1}. An absorption band at 1 645 cm^{-1} can be associated with a C-N double bond stretching vibration. The ^{13}C n.m.r. spectrum of **25** clearly shows the presence of two acetate groups (δ_C 182.21 and δ_C 168.52 with corresponding methyl carbon resonances at δ_C 25.44 and δ_C 21.24), a C-N double bond carbon resonance at δ_C 150.58, a nitrile carbon resonance at δ_C 116.94, two quaternary carbon resonances at δ_C 81.75 and δ_C 79.32, eight methine carbon resonances and a methylene carbon resonance registered at δ_C 36.43.

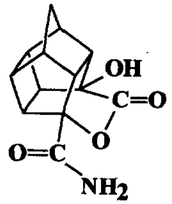
Treatment[6] of a formic acid solution of **6** with gaseous hydrochloric acid produced the amide **26.** The mass spectrum of **26** exhibits a molecular ion at m/z 247 which corresponds with a molecular formula of $C_{13}H_{13}NO_4$. The infrared spectrum is supportive of the allocated structure of **26** and displays typical N-H stretching vibration absorption bands of a NH_2-group at 3 430 cm^{-1}, a broad O-H stretching vibration absorption band around 3 280 cm^{-1}, an absorption at 1 755 cm^1 associated with the carbonyl group in the lactone ring and absorptions at 1 680 cm^{-1} (amide I band) and 1 605 cm^{-1} (amide II band) typical of an amide group. The ^{1}H and ^{13}C n.m.r. spectra of **26** also support the allocated structure. The ^{1}H n.m.r. spectrum of **26** exhibits two signals at δ_H 7.52 and δ_H 7.39 typical of the two nonequivalent protons on the nitrogen atom of the amide group due to resonance restriction of C-N rotation.



24



25



26

EXPERIMENTAL

Infrared spectra (KBr-disc) were recorded on a Nicolet 5DX FT-spectrophotometer. EI mass spectra were obtained at 70 eV on a VG 7070-E mass spectrometer. FAB mass spectra were obtained by bombardment with a 1 mA beam of 8 keV accelerated neutral xenon atoms produced by an Ion-Tech FAB gun. Melting points are uncorrected. N.m.r. spectra were recorded on a Varian Gemini-300 spectrometer.

11-Cyano-8-hydroxy-pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-lactam (6)

A solution of **1** (1 g) in water (20 cm^3) containing 0.3 cm^3 acetic acid was stirred in an ice bath for 30 min. A solution of sodium cyanide (1 g) in water (3 cm^3) was added and the reaction mixture stirred for a further 30 min. with cooling. The product was extracted with dichloromethane (100 cm^3) and the extract neutralised with sodium bicarbonate (1 g in 50 cm^3 H_2O). The excess solvent was removed under reduced pressure and the product (**6**, 1.1 g, m.p. 145°C) precipitated with petroleum ether (40-60°C) and recrystallised from acetonitrile.
ν_{max} 3 435, 3 295, 2 975, 2 245, 1 680, 1 295, 1 155, 1 115 and 1 090 cm^{-1}. EI MS, m/z 228 (M^+). FAB MS, m/z 229 ($[M+H]^+$). Calc. for $C_{13}H_{12}N_2O_2$: C, 68.42; H, 5.26; N, 12.28%. Found: C, 68.40; H, 5.23; N, 12.25%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 171.50 (S, CO), 118.23 (S, CN), 77.27 (S, C-8), 76.43 (S, C-11), 51.09 (D), 50.18 (D), 44.70 (D), 43.81 (D), 43.44 (D), 42.59 (D), 42.52 (D), 38.98 (D) and 36.25 (T). ^{1}H n.m.r. [$(CD_3)_2SO$] δ_H7.95 (NH), 6.06 (OH), 3.25-2.35 (m, 8 x H), 1.80 (d, J_{AB} = 10.8 Hz, CH_2, CH_2 : 1 x H) and 1.43 (d, J_{AB} = 10.8 Hz, CH_2 : 1 x H).

11-Amino-8-hydroxy-pentacylo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-lactam (18)

To an ice cooled mixture of 25% ammonia solution (15 cm^3), sodium cyanide (0.4 g) and ammonium chloride (0.4 g) **1** (1 g) was added in one portion and the reaction mixture was stirred for 6 h in a sealed flask immersed in ice water. The mixture was evaporated to dryness and the product (**18**, 0.9 g, m.p. 264°C) extracted on a Soxhlet apparatus with 1,4-dioxane as extractant and recrystallised from 1,4-dioxane.
ν_{max}3380, 3295, 3290, 3165, 2965, 2860, 1655, 1620, 1440, 1410, 1320, 1285, 1195, 1180, 1130, 1025, 810 and 769 cm^{-1}. EI MS, m/z 218(M^+), 190, 126, 111 and 94. Calc for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.42; N, 12.84%. Found: C, 66.04; H, 6.45; N, 12.83%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 174.37 (S, CO), 80.02 (S), 73.71

(S), 53.82 (D), 52.39 (D), 45.94 (D), 45.34 (D), 45.01 (D), 43.68 (D), 41.50 (D), 40.41 (D) and 36.66 (T). ^{1}H n.m.r. [$(CD_3)_2SO$]δ_H 7.69 (NH), 4.66 (OH), 2.54 (NH_2), 2.77 - 2.08 (m, 8 × H), 1.66 (d, J_{AB} = 10.4 Hz, CH_2: 1 × H) and 1.33 (d, J_{AB} = 10.4 Hz, CH_2: 1 × H).

*Acetylation of **18***

A solution of **18** (1 g) in anhydrous 1,4-dioxane (20 cm^3) was cooled in an ice bath and acetyl chloride (0.3 cm^3) and N,N-dimethylaniline (0.6 cm^3) added simultaneously dropwise to the reaction mixture. The reaction mixture was stirred for 10 min. with cooling and then refluxed for 1 h, cooled and diluted with water (50 cm^3) and the product (**19**, 0.8 g, m.p. 239°C) extracted with dichloromethane and recrystallised from chloroform.

ν_{max} 3295 (NH), 2975, 1750, 1685, 1665, 1550, 1430, 1370, 1235, 1175, 1150, 1040 and 750 cm^{-1}. EI MS, m/z 302 (M^+). Calc. for $C_{16}H_{18}N_2O_4$: C, 63.58; H, 5.96; N, 9.27%. Found: C, 63.56; H, 5.98; N, 9.26%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 170.36 (S, CO of lactam ring), 169.01 (S, CO of O - acetate), 168.23 (S, CO of NH - acetate), 87.02 (S, C - 8), 73.01 (S, C- 11), 66.39 (D), 50.84 (D), 49.23 (D), 44.49 (D), 42.84 (D), 41.77 (D), 40.79 (D), 39.66 (D), 36.81 (T), 23.39 (Q) and 21.44 (Q). ^{1}H n.m.r. [$(CD_3)_2SO$]δ_H 8.24 (NH), 8.22 (NH), 3.58 - 2.53 (m, 8 × H), 1.74 (d, J_{AB} = 10.5 Hz, CH_2 : 1 ×H) and 1.38 (d, J_{AB} - 10.5 Hz, CH_2: 1 × H).

*11-Cyano-8-hydroxy-pentacyclo[5.4.0.0^{2,6}.0$^{3.10}$..0^{5,9}]undecane-8,11-lactone (**20**)*

A solution of **6** (0.5 g) in dichloromethane (20 cm^3) and acetic acid (0.2 cm^3) was refluxed for 0.5 h. The reaction mixture was evaporated on a steam bath to a small volume and the product (**20**, 0.45 g, m.p. 147°C) precipitated with petroleum ether (40-60°C) and recrystallised from cyclohexane.
ν_{max} 3 395, 2 984, 2 240, 1 760, 1 155, 1 130, 1 045, 940 and 800 cm^{-1}. EI MS, m/z 229 (M^+), 201 (M^+-CO). Calc. for $C_{13}H_{11}NO_3$: C, 68.12; H, 4.80; N, 6.11%. Found: C, 68.11; H, 4.77; N, 6.09%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 172.63 (S, CO), 117.39 (S, CN), 79.12 (S, C-11), 77.45 (S, C-8), 52.12 (D), 50.25 (D), 45.08 (D), 44.44 (D), 43.78 (D), 42.55 (D), 42.25 (D), 39.74 (D) and 36.78 (T). ^{1}H n.m.r. [$(CD_3)_2SO$] δ_H 5.97 (OH), 3.30-2.50 (m, 8 x H), 1.86 (d, J_{AB} = 10.9 Hz, CH_2 : 1 x H) and 1.48 (d, J_{AB} = 10.9 Hz, CH_2: 1 x H).

*8-Hydroxy-pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-lactone-11-carboxylic acid (**21**)*

A solution of **6** (0.3 g) in hydrochloric acid (50 cm^3, 3 mol dm^{-3}) was refluxed for 15 h. The product (**21**, 0.4 g, m.p. 132°C dec.) was extracted with dichloromethane and the solvent removed under reduced pressure.
ν_{max} 3 600 - 2 425 (br), 3 445, 2 985, 1 730, 1 435, 1 360, 1 260, 1 145 and 1 065 cm^{-1}. FAB (+ ion) MS (glycerol + HCl matrix), m/z 249 ($[M+H]^+$). FAB (- ion) MS (glycerol + NaOH matrix), m/z 247 ($[M-H]^-$). Calc. for $C_{13}H_{12}O_5$: C, 62.90; H, 4.84%. Found: C, 62.87; H, 4.82%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 174.89 (S), 170.62 (S), 87.04 (S), 77.95 (S), 52.15 (D), 48.62 (D), 45.09 (D), 44.14 (D), 44.09 (D), 42.17 (D), 40.91 (D), 40.16 (D) and 36.44 (T). ^{1}H n.m.r. [$(CD_3)_2SO$] δ_H 13.25 (COOH), 5.68 (OH), 2.45 - 2.95 (m, 8 x H), 1.39 (d, J_{AB}= 10.8 Hz, CH_2: 1 x H) and 1.76 (d, J_{AB} =10.8 Hz, CH_2: 1 x H).

*Esterification of **21***

A solution of **21** (0.5 g) in absolute methanol (30 cm^3) containing concentrated sulphuric acid (0.2 cm^3) was refluxed for 1 h. The reaction mixture was poured into 50 cm^3 water and the product (0.35 g, m.p. 129°C) extracted with dichloromethane and recrystallised from 1:2 benzene-petroleum ether (60-80°C).
ν_{max} 3 485, 2 984, 2 945, 2 870, 1 760, 1 735, 1 450, 1 343, 1 295, 1 270, 1 220, 1 205, 1 145, 1 130, 1 020, 785 and 730 cm^{-1}. EI MS, m/z 262 (M^+), 234, 202, 186 and 175. Calc. for $C_{14}H_{14}O_5$: C, 64.12; H, 5.34%. Found: C, 64.11; H, 5.32%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 174.54 (S), 169.49 (S), 87.19 (S), 77.92 (S), 52.61 (Q), 52.18 (D), 48.83 (D), 45.12 (D), 44.16 (D), 44.07 (D), 42.21 (D), 40.85 (D), 40.31 (D) and 36.47 (T). ^{1}H n.m.r. [$(CD_3)_2SO$] δ_H 5.74 (OH), 3.73 (s, 1 x CH_3), 2.98 - 2.49 (m, 8 x H), 1.77 (d, J_{AB} = 10.6 Hz, CH_2: 1 x H) and 1.41(d, J_{AB} =10.6 Hz, CH_2: 1 x H).

*Acetylation of **6***

(a) A solution of **6** (0.5 g) in acetic anhydride (20 cm^3) containing sodium acetate (0.05 g) was refluxed for 1 h. The cooled reaction mixture was stirred with water (100 cm^3) for 10 h. The crystalline product (**24**, 0.45 g, m.p. 132°C) was filtered off and recrystallised from methanol.

ν_{max} 2 990, 2 245, 1 785, 1 755, 1 375, 1 245, 1 220, 1 155, 1 120, 1 080 and 1 055 cm^{-1}. EI MS, m/z 271 (M$^+$). Calc. for $C_{15}H_{13}NO_4$: C, 66.42; H, 4.79; N, 5.17%. Found: C, 66.39; H, 4.75; N, 5.15%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 168.75 (S), 166.95 (S), 116.76 (S), 82.99 (S), 79.69 (S), 50.35 (D), 49.93 (D), 44.55 (D), 43.59 (D), 42.55 (D), 42.26 (D), 41.53 (D), 39.92 (D), 36.91 (T) and 20.97 (Q). ^{1}H n.m.r. [$(CD_3)_2SO$] δ_H 3.42 (m, 1 x H), 3.24 (m, 1 x H), 3.18 (m, 2 x H), 3.00 (m, 1 x H), 2.85 (m, 2 x H), 2.75 (m, 1 x H), 2.07 (s, 1 x CH_3), 1.91 (d, J_{AB} = 11.1 Hz, CH_2: 1 x H) and 1.52 (d, J_{AB} = 11.1 Hz, CH_2: 1 x H).

(b) A solution of **6** (1 g) in anhydrous 1,4-dioxane (20 cm^3) was cooled in an ice bath and acetyl chloride (0.3 cm^3) and N,N-dimethylaniline (0.6 cm^3) added dropwise simultaneously to the reaction mixture. The reaction mixture was stirred for 10 min. with cooling and then refluxed for 1 h, cooled and diluted with water (50 cm^3) and the product (**25**, 0.85 g, m.p. 160°C) extracted with dichloromethane and recrystallised from carbon tetrachloride.

ν_{max} 3 000, 2 270, 1 765, 1 700, 1 645, 1 430, 1 265, 1 220, 1 180, 1 145, 1 120, 1 075 and 1 045 cm^{-1}. EI MS, m/z 312 (M$^+$). Calc. for $C_{17}H_{16}N_2O_4$: C, 65.39; H, 5.13; N, 8.97%. Found: C, 65.40; H, 5.12; N, 8.95%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 182.21 (S), 168.52 (S), 150.58 (S), 116.94 (S), 81.75 (S), 79.32 (S), 50.15 (D), 49.29 (D), 44.36 (D), 43.59 (D), 42.42 (D), 41.96 (D), 41.89 (D), 40.19 (D), 36.44 (T), 25.45 (Q) and 21.25 (Q). ^{1}H n.m.r. [$(CD_3)_2SO$] δ_H 3.40 (m, 1 x H), 3.24 (m, 1 x H), 3.187 (m, 2 x H), 3.00 (m, 1 x H), 2.84 (m, 2 x H), 2.74 (m, 1 x H), 2.07 (s, 1 x CH_3), 2.03 (s, 1 x CH_3), 1.88 (d, J_{AB} = 10.9 Hz, CH_2: 1 x H) and 1.49 (d, J_{AB} = 10.9 Hz, CH_2: 1 x H).

8-Hydroxy-pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-lactone-11-carboxamide (**26**)

A solution of **6** (0.5 g) in formic acid (5 cm^3) was treated with gaseous hydrochloric acid (1 litre/h.) for 6 h. at room temperature[6]. The reaction mixture was evaporated to dryness under reduced pressure and the product (**26**, 0.45 g, m.p. 187°C) recrystallised from a 1:1 water-acetone mixture.

ν_{max} 3 430, 3 280, 2 980, 1 780, 1 655, 1 605, 1 395, 1 320, 1 290, 1 255, 1 155, 1 130 and 1 045 cm^{-1}. EI MS, m/z 247 (M$^+$), 203 (M$^+$-$CONH_2$), 186 and 175. Calc. for $C_{13}H_{13}NO_4$: C, 63.16; H, 5.26; N, 5.67%. Found: C, 63.13; H, 5.24; N, 5.66%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 175.13 (S), 171.26 (S), 87.96 (S), 78.04 (S), 52.18 (D), 48.91 (D), 45.12 (D), 44.25 (D), 44.10 (D), 42.12 (D), 41.17 (D), 40.06 (D) and 36.38 (T). ^{1}H n.m.r. [$(CD_3)_2SO$] δ_H 7.52 (s, N-H_A), 7.39 (s, N-H_B), 5.68 (s, OH), 2.84 (m, 2 x H), 2.76 (m, 1 x H), 2.66 (m, 1 x H), 2.60 (m, 3 x H), 2.46 (m, 1 x H), 1.74 (d, J_{AB} = 10.6 Hz, CH_2: 1 x H) and 1.38 (d, J_{AB} = 10.6 Hz, CH_2: 1 x H).

REFERENCES

1. Martins, F.J.C.; Viljoen, A.M.; Kruger, H.G. and Joubert, J.A. *Tetrahedron*, **1993**, 49, 9573.
2. Marchand, A.P.; La Roe, W.D.; Sharma, G.V.M.; Shuri, S.C. and Reddy, D.S. *J. Org. Chem.*, **1986**, 51, 1622.
3. Dekker, J.; Dekker, J.J.; Fourie, L. and Wenteler, G.L. *J. S. Afr. Chem. Inst.*, **1975**, 28, 321.
4. Dixon, D.A.; Charlier, P.A. and Gassman, P.G. *J. Am. Chem. Soc.*,**1980**, 102, 3957.
5. Paddon-Row, M.N.; Santiago, C. and Houk, K.N. *J. Am. Chem. Soc.*, **1980**, 102, 6561.
6. Becke, F.; Fleig, H. and Pässler, P. *Liebigs Ann. Chem.*, **1971**, 749, 198.

(*Received in UK* 10 *May* 1994; *revised* 15 *July* 1994; *accepted* 22 *July* 1994)