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Synthesis of 8,11-Dihydroxy-Pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]Undecane-8,11-Lactam

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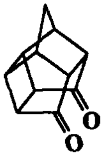
Abstract: *Treatment of pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-dione with aqueous sodium cyanide produced 8,11-dihydroxy-pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-lactam. exo-11-Cyano-11-hydroxy-pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]-8-undecanone and 5-cyano-4-oxahexacyclo-[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]-5-dodecanol were isolated as intermediates. Structures were elucidated from extensive ^{1}H and ^{13}C n.m.r. studies.*

As part of a programme that is concerned with the synthesis and chemistry of amino acids with cage structures, we have sought to synthesise α-amino acids by utilising the dione **1** as substrate in Strecker reactions. **1** is easily obtained from the Diels-Alder adduct of cyclopentadiene and p-benzoquinone by intramolecular photocyclisation.[1] Since initial cyanohydrin formation is essential for aminonitrile and subsequent amino acid formation in Strecker reactions, we decided to investigate the reaction of **1** with sodium cyanide in aqueous media. It was anticipated that the cyanohydrins **2** and/or **3** should be formed. However, the reaction unexpectedly produced a δ-lactam.



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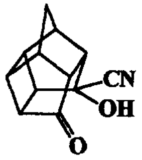

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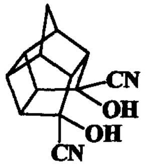

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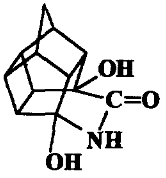

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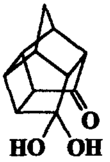

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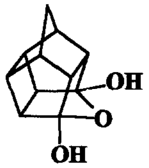

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Treatment of **1** in a solution of sodium cyanide in water for 15 h at 5°C produced on precipitation with acetone and recrystallisation from water a product of which the infrared spectrum exhibits no absorptions in the C-N triple-bond stretching region. A carbonyl group absorption is registered at 1 672 cm^{-1} and strong absorption bands appear at 3 395, 3 360 and 3 165 cm^{-1} in the O-H and N-H stretching vibration region. An elemental analysis is supportive of a molecular formula of $C_{12}H_{13}NO_3$ which was confirmed by a mass spectrum showing a molecular ion at m/z 219. Acetylation with acetic anhydride produced a tri-acetate with molecular mass of 345 as main product. On strength of the above data, as well as a ^1H and ^{13}C n.m.r. investigation, structure **4** is proposed for this product.

The 300 MHz ^1H n.m.r. spectrum of **4** shows an AB spin system for the methylene protons and five broad signals due to long range proton-proton interactions in the high field region. The peaks centred at δ_H 2.72 and δ_H 2.66 integrate for one proton each while the peaks around δ_H 2.54, δ_H 2.32 and δ_H 2.14 represent respectively two protons each. Three singlets are registered at δ_H 4.730, δ_H 6.204 and δ_H 8.133 which disappeared on treatment with D_2O and are respectively attributable to the two different hydroxyl group protons and the proton on the nitrogen atom in **4**.

The ^{13}C n.m.r. spectrum of **4** exhibits signals that can be associated with twelve different carbon atoms. A carbonylic carbon resonance is registered at δ_C 173.84. Two quaternary carbon resonances at δ_C 79.98 and δ_C 88.67 can be associated with carbon atoms bearing oxygen atoms. The rest of the ^{13}C spectrum consists of one methylene and eight methine carbon signals.

The assignments of the different resonance signals in the ^1H and ^{13}C spectra of **4** to certain nuclei are given in Table 1. The assignments were made from HETCOR and COSY 2D-experiments assisted by COLOC[2] (Correlation spectroscopy via long range couplings) and COLOC-S[3] (COLOC-selective) experiments. COLOC provides the information necessary for the assignment of remote proton-carbon coupling constant connectivities. Both direct and long-range connectivities are observed. With a COLOC-S experiment the direct connectivities are effectively suppressed and interactions between a proton and a carbon atom three bonds away are mainly observed. The hydroxyl proton resonating at δ_H 4.730 shows distinct cross peaks with the carbonyl carbon atom resonating at δ_C 173.84 (three bonds removed from the proton) and the quaternary carbon resonance at δ_C 79.98 (C-8). A correlation peak with the methine carbon resonance at δ_C 44.47 (C-7) is also observed. The hydroxyl proton resonance at δ_H 6.204 shows cross peaks with the quaternary carbon resonance at δ_C 88.67 (C-11) and long-range connectivities with the methine carbon resonances at δ_C 53.34 (C-10) and δ_C 45.30 (C-1). The NH-proton resonance at δ_H 8.133 exhibits a long-range connectivity with the quaternary carbon resonance at δ_C 79.98 (C-8) as well as a correlation with the carbonyl carbon resonance.

The quaternary carbon resonance at δ_C 88.67 (C-11) shows long-range connectivities (over three bonds) with the protons resonating at δ_H 2.536 (H-3), δ_H 2.516 (H-2), δ_H 2.297 (H-7) and δ_H 2.118 (H-9). The quaternary carbon resonance at δ_C 79.98 (C-8) shows long-range connectivities with the proton resonances at δ_H 2.656 (H-5) and δ_H 2.158 (H-10). The assignments of resonance signals to certain nuclei were verified by a COSY-experiment which shows ^1H-^1H correlation peaks between the protons on C-4 and the protons H-3 and H-5. The resonance signal of H-3 shows correlation peaks with the resonances at δ_H 2.516 (H-2) and δ_H 2.158 (H-10) whereas the resonance of H-5 correlates with the resonances at δ_H 2.715 (H-6) and δ_H 2.118 (H-9). The assignments of the ^{13}C resonance signals were made from a HETCOR experiment.

Confirmative evidence that C-11 is coupled to two different deuterium exchangeable proton bearing groups was obtained from a ^{13}C n.m.r. spectrum of **4** 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 of protons. As expected, four ^{13}C signals are registered for C-11 at δ_C88.67, δ_C 88.56, δ_C 88.58 and δ_C 88.49 corresponding to the possible four different isotopic combinations in the O-H and N-H groups coupled to C-11. The ^{13}C resonance of C-8 is registered as two double signals. The signals at δ_C 79.98 and δ_C 79.88 indicate coupling to only one hydroxyl group whereas the signals at δ_C 79.96 and δ_C 79.86 are indicative of a ß-isotopic effect from the nearby NH-

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group. Double signals due to ß-isotopic effects are also observed for the ^{13}C resonances of C-1, C-7, C-9 and C-10.

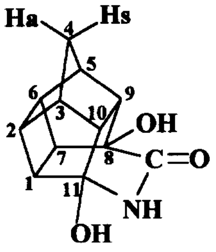

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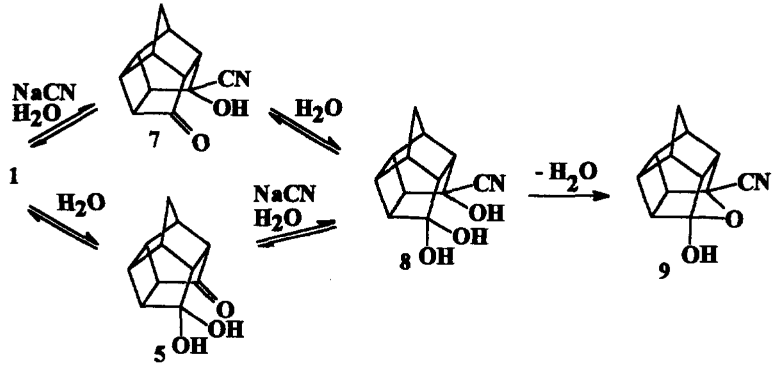
Table 1 ^{1}H and ^{13}C n.m.r. data^a of 4

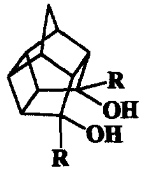
Carbon/ proton	δ_H^b(ppm)	J(Hz)	δ_C^b(ppm)	^{1}J(Hz)	>^{1}J(Hz)
1	2.348		45.30 Dd	151.0	4.1
2	2.516		43.45 Dm	148.9	
3	2.536		40.05 Dm	149.5	
4 s	1.682 d	10.5	36.94 T	131.7	
a	1.365 d	10.5			
5	2.656		45.49 Dm	148.2	
6	2.715		41.60 Dm	148.0	
7	2.297		44.47 Dd	148.5	4.8
8			79.98 Sm		
9	2.118		51.99 Dd	142.5	5.2
10	2.158		53.34 Dd	144.6	5.7
11			88.67 Sm		
NH	8.133				
OH-8	4.730				
OH-11	6.204				
C=O			173.84 Sdd		2.6;2.8

[a] 300 MHz for ^{1}H and 75 MHz for ^{13}C.

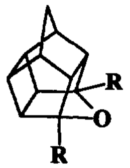
[b] Solvent $(CD_3)_2SO$ (dried over molecular sieve). Symbols in capital letters refer to patterns resulting from directly bonded protons and lower case letters to (C,H)-couplings over more than one bond. S = singlet, D or d = doublet, T or t = triplet and m = multiplet.

It was recently shown[4] that the dione **1** is easily hydrated to form the hydrates **5** and **6** in a 4:1 ratio. It can be expected that this phenomenon should play a significant role in the nucleophilic addition reactions on the carbonyl groups of **1** in aqueous media. Nucleophilic attack on the carbonyl groups in **1** or **5** is expected to take place on the *exo* face of the carbonyl groups as a result of the proximity of the groups and should lead to the formation of **8**. Transannular cyclisation of **8** is expected to form the cyclic ether **9**. It is well known[5] that *endo-endo* dihydroxy derivatives such as **10** and **11** are easily transannularly cyclised to the corresponding cyclic ethers **12** whereas compounds such as **5**, **13** and **14** (and by implication **7**) are more reluctant towards transannular cyclisations.

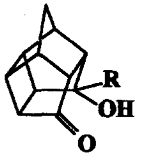




10, R=H
11, R=$NHCH_2C_6H_5$

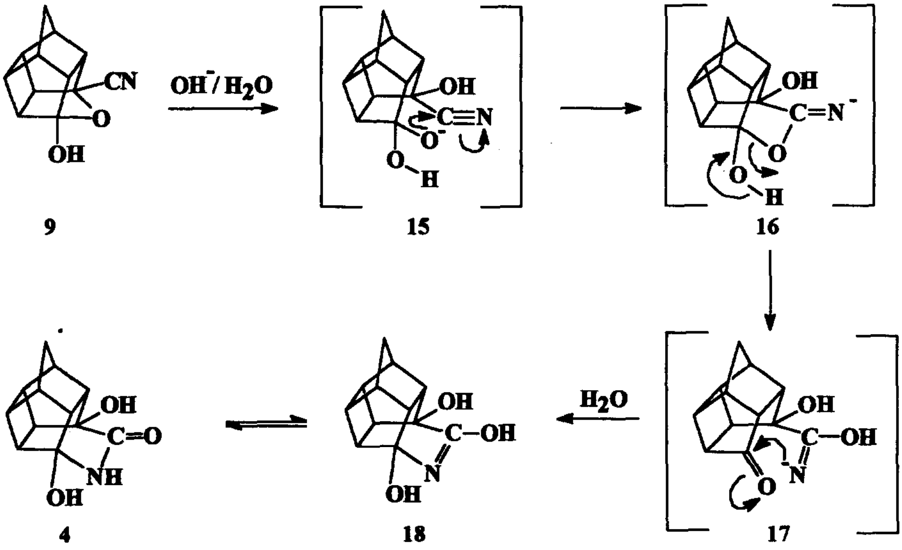


12a, R=H
b, R=$NHCH_2C_6H_5$

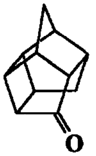


13, R=H
14, R=$NHCH_2C_6H_5$

Ring cleavage of **9** under the basic reaction conditions persistent in this reaction should result in the formation of the intermediate **15** which should instantaneously be converted to the intermediate **16**. Studies on stereomodels show that the electron deficient nitrile carbon atom of the *endo*-orientated cyano group in **15** is in an extremely favourable position to suffer attack from the nearby negatively charged oxygen atom, explaining the participation of the nitrile group in the reaction. Under similar reaction conditions nitrile groups are normally not affected. Rearrangement of **16** to **17** and subsequent cyclisation should explain the formation of the lactim **18** and the lactam **4**.



The influence of neighbouring group participation in this reaction is clearly demonstrated by the unreactivity of **19**[6] and **20**[7] towards similar reaction conditions.



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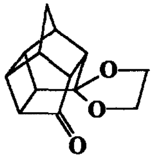

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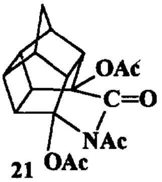

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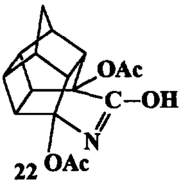

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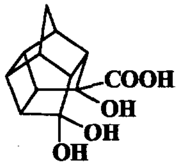
When the reaction mixture was evaporated to dryness and the product (**18**) extracted with 1,4-dioxane, the infrared spectrum differs remarkably with that of **4**. A broad absorption band is registered between 3 650 and 3 080 cm^{-1} and a sharp absorption band appears at 1 660 cm^{-1}. The mass spectrum exhibits a molecular ion at *m/z* 219 and supports an elemental analysis which suggests a molecular formula of $C_{12}H_{13}NO_3$. When dissolved in dimethyl sulphoxide for n.m.r. analysis spontaneous conversion to **4** occurred indicating a lactim-lactam tautomeric change from **18** to **4**. Acetylation of **18** with acetic anhydride indeed resulted in the formation of a 1:1 mixture of a tri-acetate (**21**) identical to the tri-acetate obtained from **4** and a di-acetate **22**. In dimethyl sulphoxide **22** is again transformed to the corresponding lactam form. (N-H proton resonance at δ_H 8.89 in DMSO-d_6 versus O-H absorption at 3 148 cm^{-1} in infrared spectrum). Recrystallisation of **18** from water also rendered **4** whereas **4** is converted to **18** upon recrystallisation from 1,4-dioxane.

None of the postulated stable intermediates could be isolated directly from the reaction mixture. In order to isolate some of the intermediates in the conversion of **1** to **4** the reaction was carried out in an acetic acid-water mixture to maintain the pH < 7. A 1:1 mixture of **7** and **9** was obtained as a precipitate after 1 h. Attempts to separate **7** and **9** failed mainly as a result of the ease of conversion of **7** to **9**. The ^{13}C n.m.r. spectrum of the mixture showed a carbonyl carbon resonance at δ_C 211.64, two nitrile carbon atom resonances at δ_C 122.00 and δ_C 119.56, two methylene carbon resonances at δ_C 37.84 and δ_C 42.98, three quaternary carbon atom resonances at δ_C 77.39, δ_C 72.56 and δ_C 119.03 (the latter is typical of a quaternary carbon coupled to two electronegative atoms and is similar to values obtained for **6**[4]) and sixteen methine carbon resonances. The ^1H n.m.r. spectrum of the mixture exhibits two hydroxyl proton resonances at δ_H 7.47 and δ_H 7.32. As expected, treatment of the mixture of **7** and **9** with an aqueous solution of sodium hydroxide produced **18** in high yield, proving that **7** and **9** indeed act as intermediates in the conversion of **1** to **4**.

In order to convert **7** and **9** to the corresponding carboxylic acids, the mixture of **7** and **9** was treated with concentrated hydrochloric acid at reflux temperature. The infrared spectrum of the product (**23**) obtained after a reaction time of 1 h exhibits a broad absorption band typical of carboxylic acids between 3 550 and 2 330 cm^{-1}. Two strong absorption bands at 3 495 and 3 330 cm^{-1} can be attributed to O-H stretching vibrations of different hydroxyl groups. A single carbonylic absorption band is registered at 1 737 cm^{-1}. The trihydroxy acid **23** is readily converted to **24** when dissolved in organic solvents such as 1,4-dioxane and dimethyl sulphoxide. Attempts to obtain n.m.r. data on **23** failed due to the dehydration to **24** in suitable solvents. The mass spectrum of **23** does not show a molecular ion at m/z 238 but instead a highest mass peak is registered at m/z 220 (M^+-H_2O).

The infrared spectrum of **24** exhibits a broad carboxylic absorption band between 3 550 and 2 435 cm^{-1}. A carbonylic absorption band appears at 1 740 cm^{-1} . An intense absorption peak at 900 cm^{-1} can be attributed to a C-O-C stretching vibration of a cyclic ether.[8] The mass spectrum showed a molecular ion at m/z 220. Esterification of **24** with methanol and concentrated sulphuric acid produced an ester of which the mass spectrum exhibits a molecular mass at m/z 234 corresponding with a molecular formula of $C_{13}H_{14}O_4$. As expected, the same ester was obtained on esterification of **23**. Further support for the structure of **24** was obtained from a ^1H and ^{13}C n.m.r. study. The n.m.r. data of **24** are given in Table 2.



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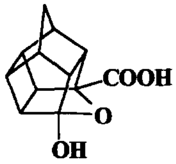

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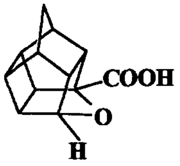

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The ^1H n.m.r. spectrum of **24** shows a carboxylic proton resonance at δ_H 12.657. A hydroxylic proton resonance is registered at δ_H 7.025. The methylene protons are registered as an AB spin system. Three broad signals appear around δ_H 2.49, δ_H 2.68 and δ_H 2.84 integrating for four, two and two protons each respectively.

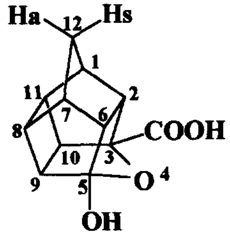

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Table 2 ^1H and ^{13}C n.m.r. data[a] of **24**

Carbon/ proton	δ_H^b(ppm)	J(Hz)	δ_C^b(ppm)	^1J(Hz)	$>^1J$(Hz)
1	2.524		45.79 Dd	143.4	7.8
2	2.809		58.32 Dm	147.6	
3			88.45 Sd		4.4
5	7.025 (OH)		117.93 Sd		4.0
6	2.506		56.14 Dm	143.9	
7	2.474		42.68 Dd	142.2	7.6
8	2.704		41.05 Dm	146.8	
9	2.444		46.30 D	149.5	
10	2.869		48.66 D	150.5	
11	2.657		41.99 Dm	146.4	
12 s	1.844 d	10.3	42.78 T	131.5	
a	1.480 d	10.3			
COOH	12.657		172.82 S		

[a] 300 MHz for ^1H and 75 MHz for ^{13}C.

[b] Solvent $(CD_3)_2SO$. Symbols in capital letters refer to patterns resulting from directly bonded protons and lower case letters to (C,H) couplings over more than one bond. S = singlet, D or d = doublet, T = triplet and m = multiplet.

The ^{13}C n.m.r. spectrum of **24** exhibits a carbonyl carbon resonance at δ_C 172.82, two quaternary carbon resonances, a methylene carbon resonance and eight methine carbon resonances. The quaternary carbon resonances at δ_C 88.45 and δ_C 117.93 can be assigned to C-3 and C-5 respectively on strength of the corresponding chemical shifts observed for **25** (δ_C 93.75)[8] and **6** (δ_C 112.23)[4]. The assignment of the different resonance signals in the ^1H and ^{13}C n.m.r. spectra of **24** to certain nuclei was made from COSY and HETCOR experiments and are given in Table 2. The assignment was supported by comparison of the chemical shifts observed for C-1, C-2, C-10 and C-11 of **25**.[8]

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.

8,11-Dihydroxy-pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-lactam (4)

A solution of **1** (1 g) in water (20 cm^3) was stirred in an ice bath for 10 min. A solution of sodium cyanide (0.4 g) in water (1 cm^3) was added dropwise over a period of 3 h and the reaction mixture stirred for a further 15 h with cooling. Precipitation with acetone, extraction of the organic compound on a Soxhlet apparatus with 1,4-dioxane as extractant and recrystallisation from water produced **4** (0.8 g, m.p. 225°C).
ν_{max} 3 395, 3 360, 3 165, 2 968, 1 672, 1 400, 1 302, 1 155, 1 015, 990, 940, 802 and 777 cm^{-1}. EI MS, m/z 219 (M$^+$), 191 (M$^+$-CO), 174 (M$^+$-CO-OH). Calc. for $C_{12}H_{13}NO_3$: C, 65.75; H, 5.94; N, 6.39%. Found: C, 65.74; H, 5.92; N, 6.37%.

8,11-Dihydroxy-pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-lactim (18)

A solution of **1** (1 g) in water (20 cm^3) was stirred in an ice bath for 10 min. A solution of sodium cyanide (0.4 g) in water (1 cm^3) was added dropwise over a period of 3 h and the reaction mixture stirred for a further 15 h with cooling. The mixture was evaporated to dryness on a steam bath and the product (**18**, 0.8 g, m.p. 245°C) extracted on a Soxhlet apparatus with 1,4-dioxane as extractant.
ν_{max} 3 415 (s), 3 650 - 3 080 (br), 2 985, 2 968, 1 660, 1 640 (sh), 1 410, 1 295, 1 145, 1 025 and 805-750 (br) cm^{-1}. EI MS, m/z 219 (M$^+$). Calc. for $C_{12}H_{13}NO_3$: C, 65.75; H, 5.95; N, 6.39%. Found: C, 65.73; H, 5.91; N, 6.38%.

Acetylation of 4

A solution of **4** (0.85 g) was refluxed in acetic anhydride (10 cm^3) for 1 h. The cooled reaction mixture was stirred with water (75 cm^3) for 10 h. The crystalline product (**21**, 0.4 g, m.p. 150°C) was filtered off and the filtrate extracted with dichloromethane. Chromatographic separation of the extract on a silica gel column with a 1:1 mixture of ethyl acetate and dichloromethane as eluant yielded **21** (0.2 g) and **22** (0.2 g, m.p. 185°C).

21 ν_{max} 2 992, 2 943, 1 745, 1 713, 1 343, 1 245, 1 155 and 1 048 cm^{-1}. EI MS, m/z 345 (M$^+$). Calc. for $C_{18}H_{19}NO_6$: C, 62.61; H, 5.51; N, 4.06%. Found: C, 62.59; H, 5.48; N, 4.01%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 172.98 (S), 169.67 (S), 169.05 (S), 168.22 (S), 95.61 (S), 85.91 (S), 49.46 (D), 48.19 (D), 45.38 (D) , 43.21 (D), 42.03 (D), 41.25 (D), 40.87 (D), 39.65 (D), 36.01 (T), 27.81 (Q), 21.29 (Q) and 21.17 (Q). ^1H n.m.r. [$(CD_3)_2SO$] δ_H 3.11 (m, 2 x H), 3.03 (m, 2 x H), 2.85 (t, J = 4.2 Hz, 1 x H), 2.74 - 2.66 (m, 3 x H), 2.33 (s, 1 x CH_3), 2.07 (s, 1 x CH_3), 2.00 (s, 1 x CH_3), 1.788 (d, J_{AB} = 11.8 Hz, ½ x CH_2) and 1.456 (d, J_{AB} = 11.8 Hz, ½ x CH_2).

22 ν_{max} 3 148 (OH), 3 000, 2 877, 1 755, 1 695, 1 375, 1 220, 1 138 and 900 cm^{-1}. EI MS, m/z 303 (M$^+$). Calc. for $C_{16}H_{17}NO_5$: C, 63.37; H, 5.61; N, 4.62%. Found: C, 63.35; H, 5.59; N, 4.59%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 169.01 (S), 168.99 (S), 167.42 (S), 93.42 (S), 86.61 (S), 50.79 (D), 49.09 (D), 44.70 (D), 43.27 (D), 42.72 (D), 41.45 (D), 40.93 (D), 39.37 (D), 37.05 (T), 21.61 (Q) and 21.36 (Q). ^1H n.m.r. [$(CD_3)_2SO$] δ_H 8.89 (s, NH), 3.35 - 2.85 (m, 4 x H), 2.77 (m, 1 x H), 2.65 - 2.50 (m, 3 x H), 2.02 (s, 1 x CH_3), 2.00 (s, 1 x CH_3), 1.774 (d, J_{AB} = 10.6 Hz, ½ x CH_2) and 1.435 (d, J_{AB} = 10.6, ½ x CH_2).

Acetylation of 18

18 (0.85 g) was treated with acetic anhydride (10 cm^3) as described above to produce **21** (0.38 g) and **22** (0.41 g).

exo-11-Cyano-11-hydroxy-pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]-8-undecanone (7) and 5-cyano-4-oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]-3-dodecanol (9)

A solution of **1** (1 g) in a mixture of water (20 cm^3) and acetic acid (1 cm^3) was stirred in an ice bath for 10 min. A solution of sodium cyanide (0.4 g) in water (2 cm^3) was added dropwise over a period of 0.5 h. The reaction mixture was stirred for a further 2 h. and the precipitated products (**7** and **9**, 1.1 g) filtered off. FAB MS (glycerol matrix), m/z 202 $(M + H)^+$.
ν_{max} 3 214 (OH), 2 516 (CN), 2 229 (CN) and 1 721 (CO) cm^{-1}. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 211.64 (S), 122.00 (S), 119.56 (S), 119.03 (S), 77.39 (S), 72.56 (S), 60.09 (D), 56.54 (D), 55.59 (D), 54.47 (D), 50.09 (D), 48.91 (D), 45.88 (D), 45.32 (D), 44.87 (D), 44.27 (D), 43.46 (D), 42.98 (T), 42.38 (D), 41.53 (D), 40.93 (D), 40.77 (D), 37.84 (T) and 35.78 (D). ^{1}H n.m.r. [$(CD_3)_2SO$] δ_H 7.47 (OH), 7.32 (OH), 3.20 - 2.25 (16 x CH), 1.896 (d, J_{AB} = 10.75 Hz, CH_2; 2 x Hs), 1.515 (d, J_{AB} = 10.75 Hz, CH_2; 2 x H_a).

Sodium hydroxide hydrolysis of 7 and 9

A solution of sodium hydroxide (0.2 g in 2 cm^3 water) was added dropwise over a period of 3 h to an ice bath cooled suspension of the mixture (1 g) of **7** and **9** in water (20 cm^3). The reaction mixture was stirred for a further 15 h with cooling. The mixture was evaporated to dryness on a steam bath and the product (**18**, 0.8 g) extracted on a Soxhlet apparatus with 1,4-dioxane as extractant.

5-Hydroxy-4-oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane-3-carboxylic acid (24)

The mixture (1 g) of **7** and **9** was treated with concentrated hydrochloric acid (10 cm^3) for 1 h under reflux conditions. The precipitated product (**23**, 0.94 g, m.p. 182°C [dec]) was filtered off and washed with ice cold water. **23** was refluxed in 1,4-dioxane (10 cm^3) for 10 min. and the solvent removed under reduced pressure to produce **24** (0.86 g, m.p. 185°C dec.) as sole product.

23 ν_{max} 3 550 - 2 330 (br), 3 495, 3 330, 2 984, 1 737, 1 343, 1 278, 1 204, 1 138, 1 081, 917 and 712 cm^{-1}. EI MS, m/z 220 (M^+-H_2O). Calc. for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92%. Found: C, 60.48; H, 5.89%.

24 ν_{max} 3 550 - 2 435 (br), 2 870, 1 740, 1 343, 1 196, 1 138, 1 073, 900, 872, 839 and 705 cm^{-1}. EI MS, m/z 220. Calc. for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49%. Found: C, 65.42; H. 5.47%.

Esterification of 23 and 24

A solution of **23** (0.24 g) or **24**(0.22 g) in absolute methanol (10 cm^3) containing concentrated sulphuric acid (0.2 cm^3) was refluxed for 0.5 h. The reaction mixture was poured into 50 cm^3 water and the product (0.18 g, m.p. 113°C) extracted with dichloromethane and recrystallised from 1:2 benzene-petroleum ether (60-80°C). Both **23** and **24** produced methyl 5-hydroxy-4-oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{8,11}]dodecane-3-carboxylate.
ν_{max} 3 394 (OH), 2 984, 1 754, 1 434, 1 352, 1 327, 1 204, 1 138, 1 089, 909 and 868 cm^{-1}. EI MS, m/z 234. Calc. for $C_{13}H_{14}O_4$: C, 66.67; H, 5,98%. Found: C, 66.65; H, 5.95%. ^{13}C n.m.r. [$(CD_3)_2SO$] δ_C 171.64 (S), 118.16 (S), 88.50 (S), 58.46 (D), 56.12 (D), 51.71 (Q), 48.79 (D), 46.32 (D), 45.79 (D), 42.82 (T), 42.71 (D), 42.00 (D), 41.12 (D). ^{1}H n.m.r. [$(CD_3)_2SO$] δ_H 7.093 (OH), 3.661 (CH_3), 2.92 - 2.82 (m, 2 x H), 2.69 (2 x H), 2.55 - 2.45 (m, 4 x H), 1.852 (d, J_{AB} = 10.4 Hz; ½ x CH_2), 1.490 (d, J_{AB} = 10.4 Hz; ½ x CH_2).

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