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# Syntheses of imido-substituted glycosans and their photocyclisation towards highly functionalised heterotricycles

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With great appreciation dedicated to Professor Gérard Descotes

**Abstract**

Reaction of *O*-protected amino-1,6-anhydro-β-D-hexopyranoses with succinic or glutaric anhydride and subsequent intramolecular acylation afforded the succinimido- and glutarimido-substituted glycosans. Irradiation with UV light of 254 nm wavelength led to γ-hydrogen abstraction at the pyranose ring by the excited carbonyl function. The stereoselective recombination of the resulting 1,4-diradicals gave annelated azetidinols, which fragmented by a retrotransannular ring opening reaction to give the glycosan-annelated azepanedione and azocanedione systems, respectively. © 2001 Published by Elsevier Science Ltd.

*Keywords:* 1,6-Anhydrosugars; Imides; Photochemistry; Azepanediones; Azocanediones

## 1. Introduction

By irradiation of an *N*-substituted succinimide with ultraviolet light of 254 nm wavelength, an excited state of the carbonyl group is generated, the properties of which are comparable to those of a diradical. The approach of the excited carbonyl function to a hydrogen atom of a substituent in suitable distance results in the abstraction of this hydrogen generating a diradical. For steric reasons, formation of a 1,4-diradical is preferred, because this γ-hydrogen abstraction proceeds via a six-membered transition state. However, electronic aspects, such as polarisation of a C–H bond by heteroatoms and the absence of a hydrogen in γ-position, can cause an abstraction of more remote hydrogen atoms, of which principally the δ-hydrogen abstraction is quite common. Subsequent recombination of the radical centres results in an intramolecular alkylation (Yang cyclisation)[1] and affords the azacyclobutanol (azetidinol) or azacyclopentanol derivative, respectively (Scheme 1). Of these, the strained azetidinol system is unstable and undergoes a fragmentation by an aza-anologous retroaldol addition to give the azepanedione system. In case of cyclic substituents, the Yang cyclisation of the diradicals proceeds stereoselectively to give the cis-annelated products, due to strain of the resulting four or five membered rings.[2–4]

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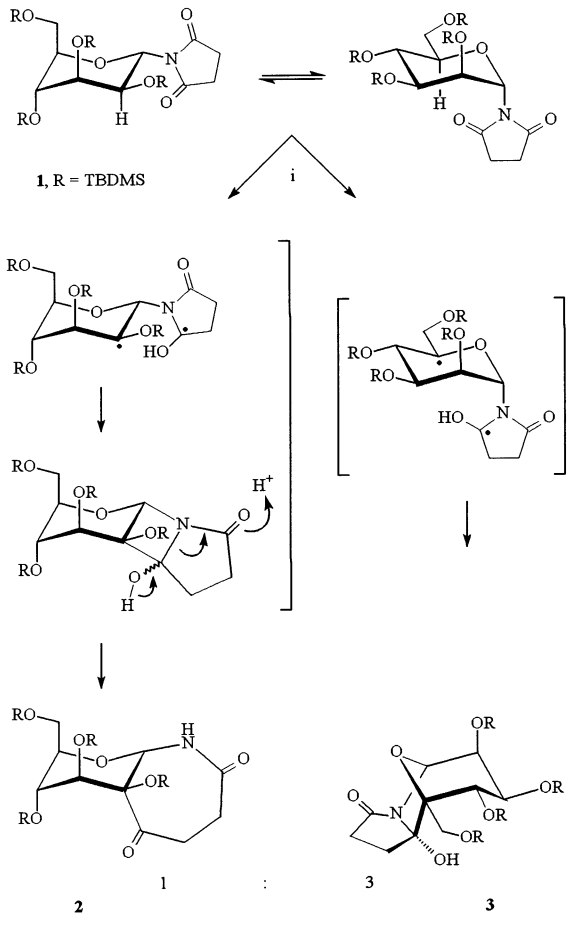
Intensive studies on photoreactions of this kind with *N*-glycopyranosyl-succinimides[5] and their 2-deoxy analogues[6,7] have revealed that the regiochemistry of the hydrogen abstraction and thus the cyclisation is distinctly controlled by stereoelectronic as well as conformational factors, caused by both the nature of the individual monosaccharide configuration and the applied protecting groups. For example, with a cis-hydrogen atom available both in the γ- as well as in the δ-position, the results of the irradiation of persilylated *N*-[α-D-mannopyranosyl]succinimide **1** are shown in Scheme 1.[5] Proceeding from the $^4C_1$(D) conformation, hydrogen abstraction from both the γ-position as well as the electronically favoured δ-position is possible, leading to the azepanedione derivative **2** and the tricyclic aminal **3**, respectively. However, the inverse anomeric effect of the succinimide substituent partly forces the pyranose chair to adopt the $^1C_4$(D) conformation, from which only the γ-hydrogen abstraction should occur. This example clearly demonstrates the influence displayed by the conformational equilibrium on the course of these photocyclisations.




Scheme 1. (i) 254 nm, $CH_3CN$, 18 °C, 3 h, **2**: 20%, **3**: 62%.

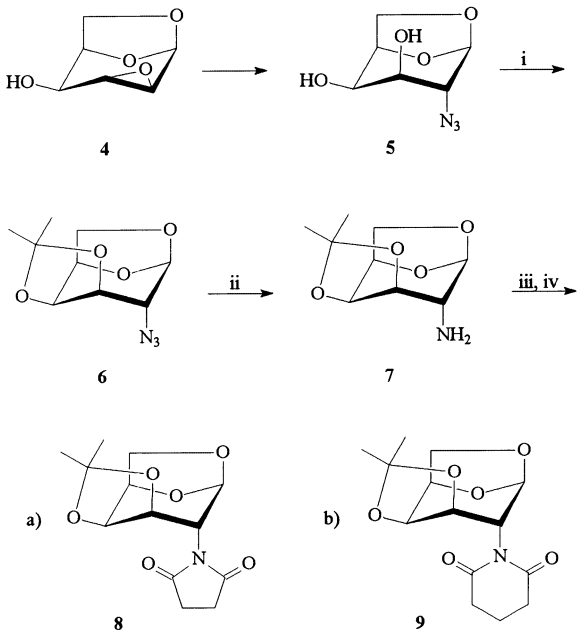
A fixation of conformation, as found in bridged systems, should dispose stronger control and hence greater predictability of the regiochemistry of the hydrogen abstraction. For example, the conformationally fixed systems of 1,6-anhydro-β-D-hexopyranoses constitute promising objects for further studies on such photochemical transformations and open a gateway to interesting heterocyclic structures. We report here the syntheses and results of irradiation of 2-imido-galactosan and 4-imido-mannosan derivatives, whereas our work with 3-imido-glucosan derivatives will be discussed separately.[8]

## 2. Results and discussion

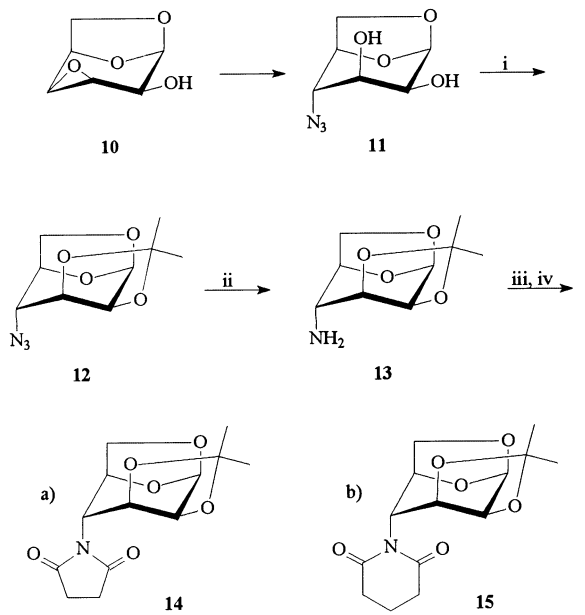
*Syntheses of Imides.*—The condensation of primary amines with dicarbonic acid anhydrides has proven to be a versatile approach to imido-substituted sugars of different kinds.[5] The amino group of a saccharide readily reacted with anhydrides such as succinic and glutaric anhydride. Under acylation conditions, the resulting amidic acids underwent a subsequent cyclisation reaction to afford the saccharide imides.

The synthesis of the 2-azido galactosan and the 4-azido mannosan started from galactosan and mannosan, respectively, and followed the pathway established by Cerny et al.[9,10] leading to 1,6;2,3-dianhydro-β-D-talopyranose **4** and 1,6;3,4-dianhydro-β-D-talopyranose **10**. Reaction of the epoxides with sodium azide[10,11] regioselectively gave the galacto-configurated 2-azido derivative **5** and the manno-configurated 4-azido derivative **11**, respectively. Due to their extremely low nucleophilicity, a short cut of the syntheses by nucleophilic epoxide ring opening with the anions of aliphatic imides such as succinimide or glutarimide was not possible.

After protection of the hydroxyl functions as photochemically inert isopropylidene acetals **6** and **12**, reduction of the azides by




Scheme 2. (i) 2,2-Dimethoxypropane, acetone, pTsOH, RT, 20 h, 73%; (ii) $H_2$, Pd/C, EtOAc–MeOH, rt, 48 h, 97%; (iii) (a) succinic anhydride, $NEt(Pr^i)_2$, rt, 20 h; (b) glutaric anhydride, $NEt(Pr^i)_2$, rt, 20 h, (iv) pyridine, $Ac_2O$ (a) rt, 20 h, 64%; (b) 100 °C, 20 h, 75%.




Scheme 3. (i) 2,2-Dimethoxypropane, acetone, pTsOH, rt, 20 h, 80%; (ii) $H_2$, Pd/C, EtOAc–MeOH, rt, 48 h, 98%; (iii) (a) succinic anhydride, $NEt(Pr^i)_2$, rt, 20 h; (b) glutaric anhydride, $NEt(Pr^i)_2$, rt, 20 h; (iii) pyridine, $Ac_2O$ (a) rt, 20 h, 69%; (b) 90 °C, 20 h, 58%.

hydrogenolysis using palladium on activated charcoal afforded the amines **7** and **13** in almost quantitative yield (Schemes 2 and 3).

Reaction of the amines **7** and **13** with ten equivalents of succinic or glutaric anhydride, respectively, in dichloromethane in the presence of *N*-ethyldiisopropylamine as auxiliary base led to the corresponding succinamidic and glutaramidic acids, respectively, which were transformed without isolation.[12] Cyclisation in the presence of acetic anhydride in pyridine afforded the saccharide succinimides **8** and **14** and glutarimides **9** and **15** in moderate to good yields. In the formation of these derivatives, the chain length of the dicarbonic acid showed a significant influence on the reaction conditions. Whereas the cyclisation of the succinamidic acids took place at room temperature, the generation of the glutarimides required higher temperatures. This effect was also observed when TBDMS ethers instead of isopropylidene acetals were applied as protecting groups (unpublished result). $^1H$ and $^{13}C$ NMR data for the unequivocal structural assignments of all new compounds **6**–**9** and **12**–**15** are summarised in Tables 1 and 2.

*Irradiations*.—All irradiations were performed with a low pressure mercury lamp at 254 nm under argon atmosphere in a solution of acetonitrile. In these transformations, up to a 1.5 g scale, no direct connection between the concentration of the solution and conversion and yield could be observed. Impurities in the starting materials may have a significant effect as inhibitors of the photoreaction though, leading to longer reaction times due to reduced rate of conversion and resulting in lower yields. Due to two other photolabile carbonyl functions, the original products were of limited stability under the reaction conditions. Thus longer reaction times resulted in an increase in decomposition products and the reaction was usually stopped after 7–9 h. Including the recovery of starting materials—usually ranging from 0 up to 20%—the yields do not exceed 90% because these reactions were always accompanied by the formation of minor amounts of side products, formed, e.g., by elimination after hydrogen abstraction to give the unsaturated saccharide and free imide. All main photoproducts crystallised very well and allowed studies of the X-ray structures of **16**, **17** and **19**. Data of these X-ray analyses are summarised in Table 3.

Table 1
$^1$H NMR chemical shifts ($\delta$ in ppm) and coupling constants ($J$ in Hz)

| Compound | H-1 | H-2 | H-3 | H-4 | H-5 | H-6a | H-6b | -C$H_2$-, succinimide | -C$H_2$-, glutarimide | –C$H_3$, isopropylidene |
|---|---|---|---|---|---|---|---|---|---|---|
| **6** [a] | 5.45, s | 3.55, s | 4.26, d | 4.42, t | 4.53, t | 4.11, d | 3.62, dd | | | 1.54, s |
| | | | $J_{3,4}$ 6.6 | $J_{4,5}$ 5.6 | $J_{5,6b}$ 5.6 | $J_{6a,6b}$ 7.6 | | | | 1.37, s |
| **7** [a] | 5.29, s | 3.14, s | 4.10, d | 4.38, t | 4.43, t | 4.14, d | 3.59, dd | | | 1.53, s |
| | | | $J_{3,4}$ 6.6 | $J_{4,5}$ 5.6 | $J_{5,6b}$ 5.6 | $J_{6a,6b}$ 7.6 | | | | 1.33,s |
| **8** [a] | 5.14, s | 4.37, s | 4.55, d | 4.80, t | 4.61, t | 4.22, d | 3.60, dd | 2.75, s | | 1.55, s |
| | | | $J_{3,4}$ 6.6 | $J_{4,5}$ 5.6 | $J_{5,6b}$ 5.6 | $J_{6a,6b}$ 7.6 | | 4 H | | 1.34, s |
| **9** [a] | 5.29, s | 5.15, s | 4.45, d | 4.78, t | 4.62, t | 4.16, d | 3.58, dd | | 2.70, t, 4 H | 1.55, s |
| | | | $J_{3,4}$ 6.6 | $J_{4,5}$ 5.6 | $J_{5,6b}$ 5.6 | $J_{6a,6b}$ 7.6 | | | 1.96, quint, 2 H | 1.34, s |
| **12** [a] | 5.35, d | 4.05, dd | 4.23, d | 3.62, s | 4.61, dd | 4.00, dd | 3.78, t | | | 1.52, s |
| | $J_{1,2}$ 3.1 | $J_{2,3}$ 6.3 | | | $J_{5,6a}$ 1.0 | $J_{6a,6b}$ 7.2 | | | | 1.32, s |
| | | | | | $J_{5,6b}$ 6.3 | | | | | |
| **13** [a] | 5.31, d | 4.06–4.03, | 4.10, d | 3.21, s | 4.41, dd | 4.06–4.03, | 3.76, t, | | | 1.54, s |
| | $J_{1,2}$ 2.5 | m | $J_{2,3}$ 6.1 | | $J_{5,6a}$ 1.0 | m | $J_{6a,6b}$ 6.6 | | | 1.31, s |
| | | | | | $J_{5,6b}$ 6.6 | | | | | |
| **14** [b] | 5.40, d | 4.35, dd | 4.50, d, | 4.17, s | 4.39, d | 3.95, d, | 3.67, dd | 2.67, s | | *1.48*, s |
| | $J_{1,2}$ 2.8 | $J_{2,3}$ 6.0 | | | $J_{5,6b}$ 6.3 | $J_{6a,6b}$ 7.1 | | 4 H | | 1.27, s |
| **15** [a] | 5.42, d | 4.51, dd | 4.43, d | 4.78, s | 4.26, d | 4.04, d | 3.72, t | | 2.68, t, 4 H | 1.50, s |
| | $J_{1,2}$ 3.1 | $J_{2,3}$ 6.3 | | | $J_{5,6b}$ 6.3 | $J_{6a,6b}$ 6.3 | | | 1.95, quint, 2 H | 1.27, s |

[a] Solvent: $CDCl_3$.
[b] Solvent: $d_6$-$Me_2SO$.

Considering the synthesised imido derivatives of D-galactosan (**8**, **9**) and D-mannosan (**14**, **15**) and assuming γ-hydrogen abstraction, there are in each case two suitable hydrogen atoms which could react with the excited carbonyl function. One of these is bound to a bridgehead atom (H-1 for the galacto cases, H-5 for the manno cases) which makes an abstraction less favourable compared to the other one, the H-3 in both configurations. However, a δ-hydrogen abstraction of H-4 for the galacto cases and H-2 for the manno cases cannot entirely be excluded. Again, there is no significant polarisation of these C–H bonds which could render such a remote hydrogen abstraction favoured. Thus, the alkylation at C-3 for both sugar configurations is expected to be the most probable course of these photoreactions (Scheme 4).

Irradiation of the succinimido derivative **8** was not completed after 9 h, and in addition to 75% of the expected azepanedione **16**, 14% of starting material was recovered. Furthermore, a small amount of elimination product was indicated by TLC. The $^1$H NMR of **16** showed the NH-signal at $\delta$ 6.19, the splitting of the succinimide $CH_2$-groups into an ABCD spin system and no signal for H-8. The $^{13}$C NMR displayed the typical signals of the amide group ($\delta_C$ 174.81) and the keto function ($\delta_C$ 207.14). Furthermore, there was a new quaternary carbon atom at $\delta_C$ 83.46 (C-8), and the former identical secondary carbon atoms of the succinimide now gave two signals at $\delta_C$ 36.48 (C-6) and $\delta_C$ 29.97 (C-5). The coupling constants of the sugar system ($J_{1,2}$ and $J_{9,10}$) in the tricyclic structure were unchanged compared to the starting bicyclic form, which indicated that the pyranose ring still adopted a $^1C_4$(D) chair conformation. This was confirmed by the X-ray structure shown as an ORTEP drawing in Fig. 1. Attached to this chair, the seven-membered ring adopted a boat conformation.

In case of the irradiation of the glutarimido derivative **9**, TLC indicated the formation of two products with very similar $R_f$-values and little elimination product. Again, 12% of the starting material was recovered. The azocanedione **17**, expected as the product of γ-hydrogen abstraction and cis-alkylation at C-3 of the galactosan, was found to be the main product, and was obtained in a yield of 58%. Unfortunately, a second product in a $^1$H NMR estimated amount of 14% could not be separated from **17** in a state pure enough to

Table 2
$^{13}$C NMR chemical shifts ($\delta$ in ppm)

| Compound | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 | Succinimide | Glutarimide | Isopropylidene |
|---|---|---|---|---|---|---|---|---|---|
| **6** [a] | 99.86 | 61.40 | 73.62 | 69.40 | 72.28 | 63.59 | | | 109.07<br>25.71, 24.38, –*C*H$_3$ |
| **7** [a] | 102.74 | 53.81 | 77.68 | 69.30 | 72.52 | 63.55 | | | 108.55<br>25.80, 24.40, –*C*H$_3$ |
| **8** [a] | 100.12 | 54.00 | 72.54 | 69.44 | 71.38 | 63.54 | 176.26, C=O<br>28.09, –*C*H$_2$– | | 25.84, 24.42, –*C*H$_3$ |
| **9** [a] | 101.15 | 54.98 | 72.83 | 69.34 | 72.21 | 62.74 | | 172.19, C=O<br>33.30, 2 C, –*C*H$_2$–<br>16.87, –*C*H$_2$ | 108.15<br>25.80, 24.40, –*C*H$_3$ |
| **12** [a] | 99.47 | 72.19 | 73.73 | 60.17 | 73.97 | 65.31 | | | 110.31<br>25.90, 25.81, –*C*H$_3$ |
| **13** [a] | 99.57 | 72.11 | 78.06 | 52.34 | 76.52 | 65.51 | | | 109.99<br>25.94, 25.87, –*C*H$_3$ |
| **14** [b] | 98.77 | 72.32 | 71.91 | 52.12 | 74.10 | 65.91 | 177.41, C=O<br>28.21, –*C*H$_2$– | | 108.74<br>26.12, 26.03, –*C*H$_3$ |
| **15** [a] | 99.57 | 72.30 | 73.60 | 54.25 | 75.77 | 67.03 | | 172.43, C=O<br>33.38, 2 C, –*C*H$_2$–<br>16.86, –*C*H$_2$– | 109.04<br>25.95, 25.85, –*C*H$_3$ |

[a] Solvent: $CDCl_3$.
[b] Solvent: $d_6$-$Me_2SO$.

Table 3
Crystal data, data collection parameters and refinement results

| | **16** [b] | **17** [a] | **19** [a] |
|---|---|---|---|
| Formula | $C_{13}H_{17}NO_6$ | $C_{14}H_{19}NO_6$ | $C_{14}H_{19}NO_6$ |
| Formula weight | 283.28 | 297.30 | 297.30 |
| Crystal dimension (mm) | | $0.7\times0.5\times0.2$ | $0.7\times0.3\times0.3$ |
| Crystal system | monoclinic | monoclinic | orthorhombic |
| Space group | $P2_1$ (no.4) | $P2_1$ (no.4) | $P2_12_12_1$ (no. 19) |
| $a$ (Å) | 8.6124(18) | 8.4493(13) | 8.5471(7) |
| $b$ (Å) | 7.6762(16) | 9.6356 (14) | 10.7122(13) |
| $c$ (Å) | 10.883(2) | 9.2656(11) | 15.187(3) |
| $\alpha$ (°) | 90 | 90 | 90 |
| $\beta$ (°) | 111.456(3) | 114.704(12) | 90 |
| $\gamma$ (°) | 90 | 90 | 90 |
| $V$ (Å$^3$) | 669.6(2) | 685.31(17) | 1390.5(3) |
| Cell weight | 566.55 | 594.60 | 1189.21 |
| $Z$ | 2 | 2 | 4 |
| $\rho_{calcd}$ (g cm$^{-3}$) | 1.4050(4) | 1.441 | 1.4202(3) |
| $F(000)$ | 300 | 316 | 632 |
| Radiation | Mo K$\alpha$ | Cu K$\alpha$ | Cu K$\alpha$ |
| $\lambda$ (pm) | 71.073 | 154.178 | 154.178 |
| $\mu$ (mm$^{-1}$) | 0.112 | 0.954 | 0.940 |
| $T$ (°C) | −120 | −100 | 20 |
| $2\theta_{max}$ (°) | 54.90 | 152.80 | 152.85 |
| Unique reflexions | 2949 | 1527 | 2155 |
| Observed reflexions | 2869 | 1525 | 2126 |
| $R$ | 0.0467 | 0.0385 | 0.0389 |
| $wR^2$ | 0.1185 | 0.1025 | 0.1008 |
| Flack parameter | −0.2(8) | 0.0492 | 0.0371 |
| $S$ = Goodness-of-fit | 1.053 | 1.057 | 1.087 |

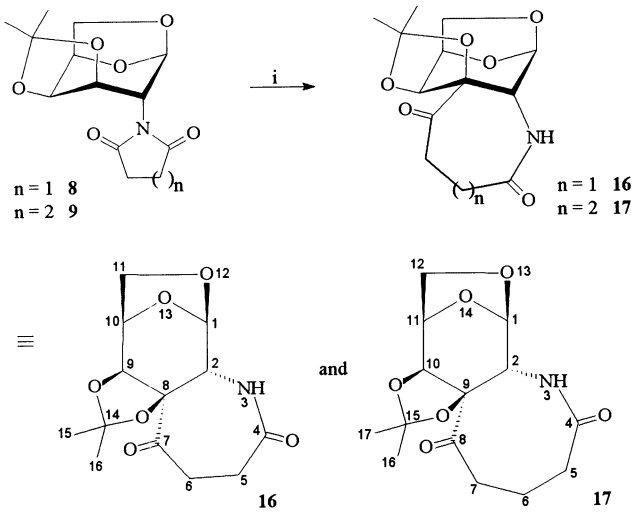
[a] Enraf–Nonius CAD-4 diffractometer.
[b] Bruker Apex-diffractometer.

get proper NMR spectra. Although it has not been identified so far, the $^{13}C$ NMR tentatively referred to a system with both a lactam structure and a keto function as well. Thus, hydrogen abstraction and cyclisation at the bridgehead C-1 must be assumed.

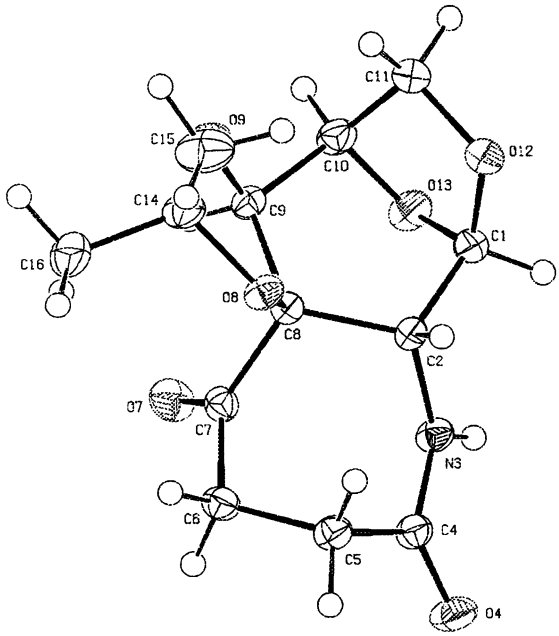
NMR data for a decisive structural assignment of **17** were the signals of the lactam and carbonyl function (NH–C=O doublet at $\delta$ 5.41, $\delta_C$ 174.22, C=O $\delta_C$ 210.07), the signal of the new quaternary centre C-9 at $\delta_C$ 87.61 and the splitting of the methylene groups of the former glutarimide system (C-7 $\delta_C$ 37.25, C-5 $\delta_C$ 34.08 and C-6 $\delta_C$ 23.27).

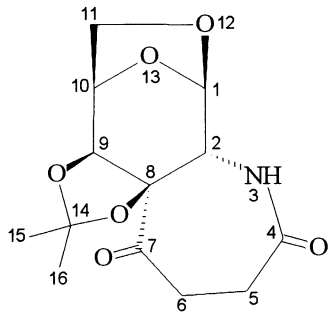
Again, no significant changes concerning the coupling constants of the sugar system $J_{1,2}$ and $J_{10,11}$ were observed, which indicated a pyranose chair conformation. The structure of **17** elucidated by NMR experiments was proven by X-ray structure analysis, the ORTEP drawing shown in Fig. 2. Inspection revealed a kind of chair–boat conformation for the eight-membered ring annelated to the sugar ring in $^1C_4$ chair conformation.

The photoreaction of the succinimido-substituted mannosan derivative **14** proved to be more straightforward. After 7 h, complete conversion of the starting material was observed and the azepandione **18** was obtained in 85% yield. The structure was elucidated by NMR experiments, displaying the typical signals of the amide group (NH–C=O doublet at $\delta$ 5.77, $\delta_C$ 173.36) and the keto function ($\delta_C$ 204.77). The signal of a new quaternary centre (C-8 $\delta_C$ 84.37) was in keeping with the absence of the signal of H-8. Furthermore, the singlet of the succinimide protons split into an ABCD-system, their carbon centres appearing at $\delta_C$ 33.39 (C-6) and $\delta_C$ 29.96 (C-5). The unchanged coupling constants of the sugar system ($J_{1,2}$ and $J_{9,10}$) indicated that the chair conformation of the pyranose ring was not affected by the annelated seven-membered ring (Scheme 5).



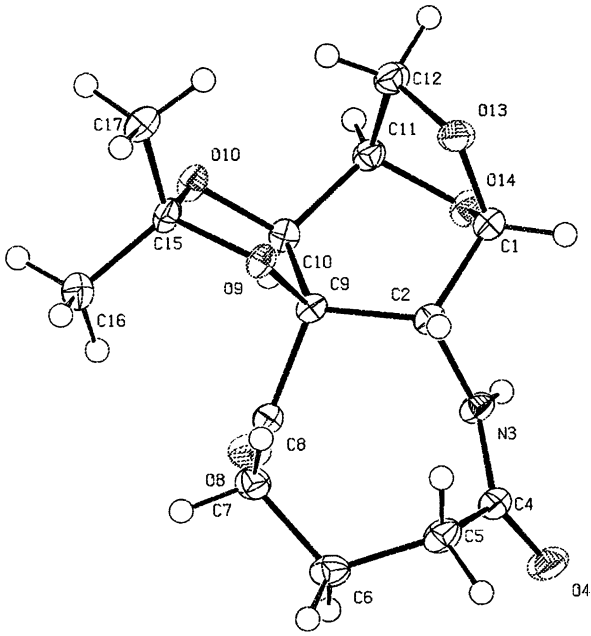

Scheme 4. (i) 254 nm, MeCN, 18 °C, **16**: 9 h, 75%, **17**: 7.5 h, 58%.

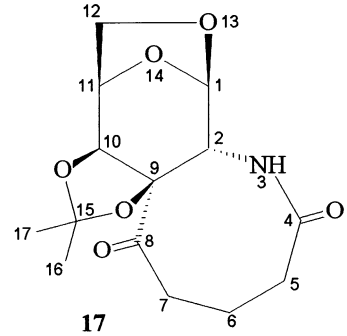



**16**

Fig. 1. ORTEP drawing of **16**.

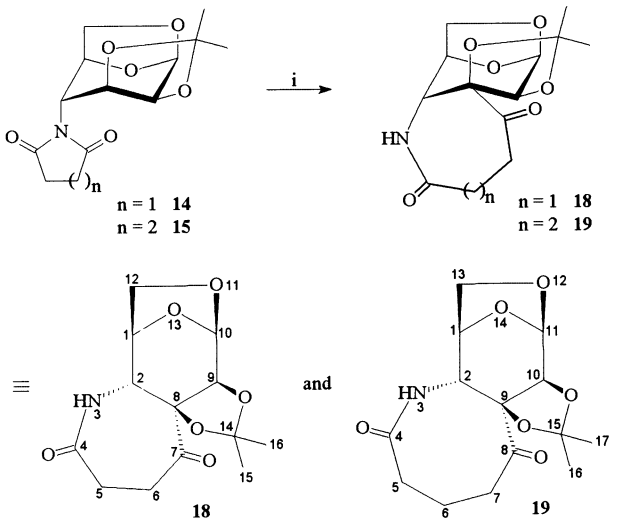



**17**

Fig. 2. ORTEP drawing of **17**.

Irradiation of the glutarimido derivative **15** was terminated after 8 h and afforded 73% of the azocanedione system **19** as well as 16% of recovered starting material. Elimination only led to trace amounts of unsaturated mannosan derivative. Characteristic NMR data of the tricyclic system **19** were the signals of the carbonyl group at $\delta_C$ 208.52 and the lactam system (NH–C=O, doublet at $\delta$ 5.80 and $\delta_C$ 173.93). Furthermore, the new quaternary centre C-9 gave a signal at $\delta_C$ 87.75 and the secondary centres of the former glutarimide system appeared at $\delta_C$ 36.46 (C-7), $\delta_C$ 34.39 (C-5) and $\delta_C$ 24.09 (C-6). Likewise all other tricycles examined, the coupling constants ($J_{1,2}$ and $J_{10,11}$) displayed that the annelated ring did not have significant influence on the conformation of the pyranose chair. X-ray struc-




Scheme 5. (i) 254 nm, MeCN, 18 °C, **18**: 7 h, 85%, **19**: 8 h, 73%.

ture analysis of **19** verified these results and is shown as an ORTEP drawing in Fig. 3. Again, the $^1C_4$ pyranose chair is annelated to the eight-membered ring, however, in this case a sort of crown (chair–chair) conformation was observed.

The azepanedione system in principle is an interesting structural element as it is widespread in physiologically active compounds in which only minor structural changes induce significantly diverse effects.[13,14] Additionally, these heterotricycles constitute interesting objects as precursors to branched chain sugars.[15] The chemical transformations of the azepanediones **16** and **18** and the azocanediones **17** and **19** such as *N*-protection with subsequent lactam opening or cleavage of the 1,6-anhydro bridge bear some exciting structures, which in turn open new potentials of chemical modifications and structure design, and offer versatile access to variably functionalised heterocycles and higher sugar derivatives.

## 3. Experimental

*General methods.*—TLC was performed on Silica Gel 60-coated aluminium sheets (E. Merck) using the given eluent mixtures. Spots were visualised under UV light at 366 nm and by spraying with 10% $H_2SO_4$ in EtOH and subsequent heating. Column chromatography was performed on Silica Gel 60 (230–240 mesh, grain size 0.040–0.063 nm, E. Merck). Petroleum ether refers to the fraction with distillation range 50–70 °C. All irradiations were performed in commercial dry MeCN (Fluka), deoxygenated by 30 min degassing with Ar in an ultrasonic bath. A 60 Watt

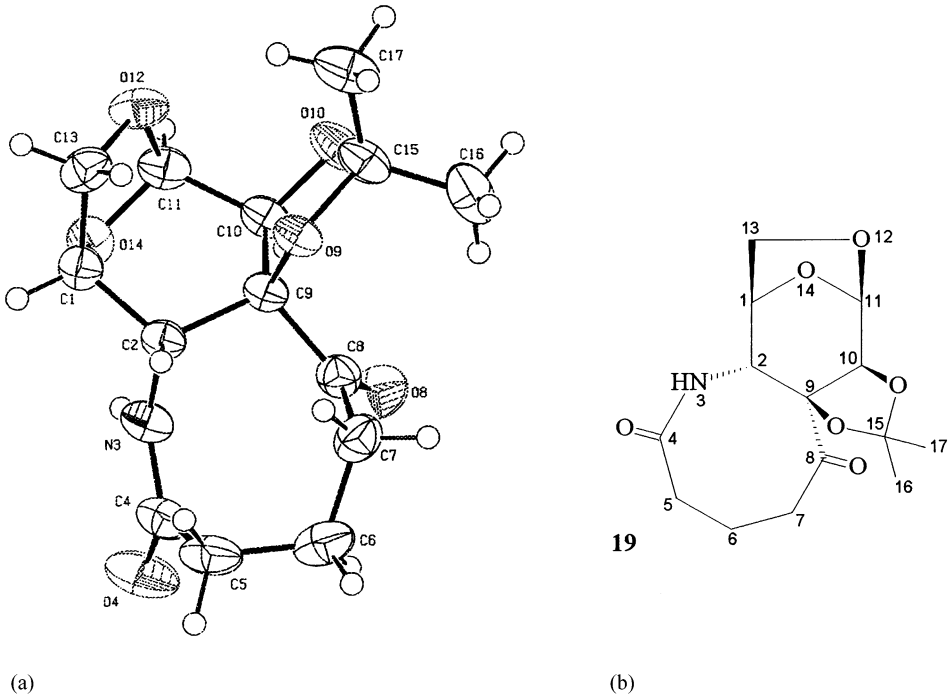



Fig. 3. ORTEP drawing of **19**.

low-pressure mercury vapour lamp of the company Heraeus ($\lambda = 254$ nm) was used. The photo reactor was made of quartz glass and measured 35 cm in length and 4.5 cm in diameter, and the temperature was maintained at 18 °C by water cooling. Melting points were measured on a ST-apotec and are reported uncorrected. Optical rotations were measured on a Perkin–Elmer Polarimeter 243, with $[\alpha]_D$ values given in units of $10^{-1}$ deg cm$^2$ g$^{-1}$. Elemental analyses were performed by the microanalytical laboratory of the Institute of Organic Chemistry of the University of Hamburg. IR absorptions were recorded on a ATI Matteson FTIR (Genesis Series). NMR spectra were recorded on a Bruker AMX-400 NMR spectrometer. Chemical shifts are referred to the solvent used.

*Procedure A: isopropylidenation.*—The diol (50 mmol) was dissolved in acetone (100 mL) and 2,2-dimethoxypropane (50 mL) and treated with catalytic amounts of 4-toluene sulfonic acid. After stirring overnight at rt, the reaction was quenched by addition of triethylamine (5 mL) and concentrated under reduced pressure. The residue was taken up in $CH_2Cl_2$ or $Et_2O$ and washed with aq satd $NaHCO_3$ solution and brine. Drying and evaporation of the solvent left the crude product, which was purified by column chromatography using the quoted eluent.

*Procedure B: hydrogenation.*—The azide (20 mmol) was dissolved in a mixture of dry EtOAc (100 mL) and dry MeOH (25 mL) and hydrogenated using Pd/C (10 %) (10% by weight) by stirring at rt under one atmosphere of hydrogen for 2 days. Removal of the catalyst by filtration through a short pad of Celite and evaporation of the solvents yielded the amine, which was transformed without further purification.

*Procedure C: imide formation.*—A suspension of the amine (10.0 mmol), succinic anhydride (10.0 g, 100.0 mmol) or glutaric anhydride (11.4 g, 100.0 mmol) and *N*-ethyldiisopropylamine (1.7 mL, 10.0 mmol) in dry $CH_2Cl_2$ (75 mL) was stirred overnight at rt. After addition of MeOH (10 mL), the solvents were evaporated under reduced pressure. The residue was dissolved in dry pyridine (30 mL) and $Ac_2O$ (30 mL) and stirred overnight at the quoted temperature. The reaction mixture was concentrated under reduced pressure and codestilled twice with toluene. The residue was taken up in $CH_2Cl_2$, neutralised with aq satd $NaHCO_3$ solution and washed with brine. Drying and evaporation of the solvent afforded the crude product, which was purified by column chromatography using the quoted eluent and if necessary by subsequent recrystallisation.

*Procedure D: irradiation.*—The imido-substituted sugar (0.5–1.0 g) was dissolved in dry, deoxygenated MeCN (200 mL) and irradiated at 18 °C under an Ar atmosphere for 7–9 h. Purification was performed by column chromatography using the quoted eluent and by subsequent recrystallisation.

*1,6-Anhydro-2-azido-2-deoxy-3,4-*O*-isopropylidene-β-*D*-galactopyranose* (**6**).—1,6-Anhydro-2-azido-2-deoxy-β-D-galactopyranose (**5**, 5.70 g, 30.39 mmol) was protected following Procedure A. Column chromatography with 12:1 petroleum ether–EtOAc yielded compound **6** (5.01 g, 73%) as white crystals: mp 38 °C, $[\alpha]_D^{20}$ −25.8° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_9H_{13}N_3O_4$: C, 47.57; H, 5.77; N, 18.49. Found: C, 48.00; H, 5.84; N, 17.96.

*2-Amino-1,6-anhydro-2-deoxy-3,4-*O*-isopropylidene-β-*D*-galactopyranose* (**7**).—Reduction of azide **6** (4.0 g, 17.60 mmol) according to Procedure B provided the amine **7** (3.43 g, 97%) as a hygroscopic, colourless solid which was transformed without further purification.

*1,6-Anhydro-2-deoxy-3,4-*O*-isopropylidene-2-*N*-succinimido-β-*D*-galactopyranose* (**8**).—The amine **7** (2.0 g, 9.94 mmol) was reacted with succinic anhydride according to Procedure C, with the cyclisation step completed after stirring overnight at room temperature. Column chromatography using 3:1 petroleum ether–ethylacetate as eluent yielded the pure product, which was furthermore recrystallised from 2-propanol to give compound **8** (1.80 g, 64%) as white needles: mp 209–211 °C, $[\alpha]_D^{20}$ +21.5° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05; N, 4.94. Found: C, 54.74; H, 5.99; N: 4.69.

*1,6-Anhydro-2-deoxy-2-*N*-glutarimido-3,4-*O*-isopropylidene-β-*D*-galactopyranose* (**9**).—The amine **7** (2.0 g, 9.94 mmol) was reacted

with glutaric anhydride according to Procedure C, with the cyclisation step requiring 20 h at 100 °C. Column chromatography using 3:1 petroleum ether–ethylacetate yielded the pure product **9** (2.21 g, 75%) which was furthermore crystallised from 2-propanol to give colourless, prismatic crystals: mp 213 °C, $[\alpha]_D^{20}$ + 3.7° (*c* 0.79, $CHCl_3$). Anal. Calcd for $C_{14}H_{19}NO_6$: C, 56.56; H, 6.44; N, 4.71. Found: C, 56.38; H, 6.45; N, 4.50.

*1,6-Anhydro-4-azido-4-deoxy-2,3-*O*-isopropylidene-β-*D*-mannopyranose* (**12**).—1,6-Anhydro-4-azido-4-deoxy-β-D-mannopyranose (**11**, 6.0 g, 32.06 mmol) was protected according to Procedure A. Column chromatography using 12:1 petroleum ether–EtOAc afforded compound **12** (5.83 g, 80%) as a white solid: mp 49 °C, $[\alpha]_D^{20}$ − 111.7° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_9H_{13}N_3O_4$: C, 47.57; H, 5.77; N, 18.49. Found: C, 47.97; H, 5.82; N, 18.16.

*4-Amino-1,6-anhydro-4-deoxy-2,3-*O*-isopropylidene-β-*D*-mannopyranose* (**13**).—The azide **12** (3.6 g, 15.84 mmol) was hydrogenated following Procedure B and the amine **13** (3.12 g, 98 %) was obtained as a hygroscopic, colourless solid which was transformed without further purification: mp 77–79 °C, $[\alpha]_D^{20}$ − 40.3° (*c* 1.0, $CHCl_3$).

*1,6-Anhydro-4-deoxy-2,3-*O*-isopropylidene-4-*N*-succinimido-β-*D*-mannopyranose* (**14**).—Compound **13** (2.5 g, 12.42 mmol) was reacted with succinic anhydride according to Procedure C, with the cyclisation step carried out by stirring overnight at rt. The crude product was purified by column chromatography using 3:1 petroleum ether–EtOAc as eluent and subsequent crystallisation from 2-propanol to give compound **14** (2.43 g, 69%) as white crystals: mp 187–189 °C, $[\alpha]_D^{20}$ − 93.5° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05; N, 4.94. Found: C, 55.20; H, 6.09; N, 4.79.

*1,6-Anhydro-4-deoxy-4-*N*-glutarimido-2,3-*O*-isopropylidene-β-*D*-mannopyranose* (**15**).—Compound **13** (2.0 g, 9.94 mmol) was reacted with glutaric anhydride according to Procedure C, with the cyclisation step requiring 90 °C for 20 h. The crude product was purified by column chromatography using 3:1 petroleum ether–EtOAc as eluent and subsequent crystallisation from 2-propanol to give compound **15** (1.71 g, 58%) as white needles: mp 137–138 °C, $[\alpha]_D^{20}$ − 118.9° (*c* 1.5, $CHCl_3$). Anal. Calcd for $C_{14}H_{19}NO_6$: C, 56.56; H, 6.44; N, 4.71. Found: C, 56.55; H, 6.67; N, 4.33.

*(1*R*,2*R*,8*R*,9*S*,10*R*)-8,9-Isopropylidenedioxy-12,13-dioxa-3-aza-tricyclo[8.2.1.0$^{2,8}$]tridecan-4,7-dione* (**16**).—The succinimido derivative **8** (0.99 g, 3.49 mmol) was irradiated according to Procedure D for 9 h. Purification by column chromatography with 3:1–1:1 petroleum ether–EtOAc yielded recovered starting material (0.13 g, 14%) and compound **16** (0.74 g, 75%) as a white solid, which can be crystallised from 2-propanol to give colourless needles: mp 272–275 °C, $[\alpha]_D^{20}$ + 1.7° (*c* 1.0, $CHCl_3$), $^1$H NMR ($CDCl_3$): $\delta$ 6.19 ($s_b$, 1 H, NH), 5.38 (s, 1 H, H-1), 5.26 (d, 1 H, $J_{9,10}$ 7.1 Hz, H-9), 4.78 (dd, 1 H, $J_{10,11b}$ 4.6 Hz, H-10), 4.29 (d, 1 H,, $J_{11a,11b}$ 7.6 Hz, H-11a), 3.90 (d, 1 H, $J_{2,NH}$ 5.1 Hz, H-2), 3.57 (dd, 1 H, H-11b), 3.22–3.11 (m, 2 H, H-6a, H-5a), 2.67 (m, 1 H, H-6b), 2.45 (m, 1 H, H-5b), 1.53, 1.19 (both s, both 3 H, –C$H_3$, isopropylidene), $^{13}$C NMR ($CDCl_3$): $\delta$ 207.14 (C=O), 174.81 (NH–C=O), 110.56 (isopropylidene, 99.78 (C-1), 83.46 (C-8), 72.48 (C-10), 67.85 (C-9), 63.34 (–$CH_2$–, C-11), 60.98 (C-2), 36.48 (–$CH_2$–, C-6), 29.97 (–$CH_2$–, C-5), 26.81, 25.81 (both –$CH_3$, isopropylidene). Anal. Calcd for $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05; N, 4.94. Found: C, 54.88; H, 6.08; N, 4.89.

*(1*R*,2*R*,9*R*,10*S*,11*R*)-9,10-Isopropylidenedioxy-13,14-dioxa-3-aza-tricyclo[9.2.1.0$^{2,9}$]tetradecan-4,8-dione* (**17**).—Irradiation of the glutarimido derivative **9** (0.99 g, 3.33 mmol) according to Procedure D for 7.5 h and purification by column chromatography using 3:1–1:2 petroleum ether–EtOAc gave recovered starting material (0.12 g, 12%), impurified, unidentified side product (0.14 g, 14%) and compound **17** (0.57 g, 58%) as a white solid, which was crystallised from 2-propanol as colourless, prismatic crystals: mp 218 °C, $[\alpha]_D^{20}$ + 44.9° (*c* 0.65, $CHCl_3$), $^1$H NMR ($CDCl_3$): $\delta$ 5.41 (d, 1 H, $J_{2,NH}$ 10.7 Hz, NH), 5.38 (s, 1 H, H-1), 5.09 (d, 1 H, $J_{10,11}$ 6.6 Hz, H-10), 4.62 (dd, 1 H, $J_{11,12b}$ 4.5 Hz, H-11), 4.37 (d, 1 H, $J_{12a,12b}$ 7.6 Hz, H-12a), 4.08 (d, 1 H, H-2), 3.64 (dd, 1 H, H-12b), 3.42 (m, 1 H, H-7a), 2.54–2.40 (m, 2 H, H-5a, H-5b), 2.26 (m, 1 H, H-7b), 2.15 (m, 1 H, H-6a), 2.03 (m, 1 H,

H-6b), 1.60, 1.17 (both s, both 3 H, –C$H_3$, isopropylidene), $^{13}$C NMR ($CDCl_3$): $\delta$ 210.07 (C=O), 174.22 (NH–C=O), 110.74 (isopropylidene), 100.40 (C-1), 87.61 (C-9), 72.45 (C-11), 68.15 (C-10), 65.02 (–$C$H$_2$–, C-12), 54.75 (C-2), 37.25(–$C$H$_2$–, C-7), 34.08 (–$C$H$_2$–, C-5), 27.19, 26.74 (both –$C$H$_3$, isopropylidene), 23.27 (–$C$H$_2$–, C-6). Anal. Calcd for $C_{14}H_{19}NO_6$: C, 56.56; H, 6.44; N, 4.71. Found: C, 56.17; H, 6.45; N, 4.51.

*(1*R*,2*R*,8*S*,9*S*,10*R*) - 8,9 - Isopropylidene-dioxy - 11,13 - dioxa - 3 - aza - tricyclo[8.2.1.0$^{2,8}$]-tridecan-4,7-dione* (**18**).—The succinimido derivative **14** (0.73 g, 2.59 mmol) was irradiated according to Procedure D for 7 h. Purification by column chromatography with 1:1–1:2 petroleum ether–EtOAc yielded compound **18** (0.62 g, 85%) as a white solid, which can be crystallised from 2-propanol or MeOH to give fine white needles: mp 265–269 °C (dec), $[\alpha]_D^{20}$ −47.6° (*c* 0.72, MeOH), $^1$H NMR ($CDCl_3$): $\delta$ 5.77 (d, 1 H, $J_{2,NH}$ 5.0 Hz, NH), 5.54 (d, 1 H, $J_{9,10}$ 3.8 Hz, H-10), 4.87 (d, 1 H, H-9), 4.55 (d, 1 H, $J_{1,12b}$ 6.3 Hz, H-1), 4.09–4.05 (m, 2 H, H-2, H-12a), 3.91 (dd, 1 H, $J_{12a,12b}$ 7.6 Hz, H-12b), 3.28 (m, 1 H, H-6a), 3.12 (m, 1 H, H-5a), 2.67 (m, 1 H, H-6b), 2.57 (m, 1 H, H-5b), 1.56, 1.19 (both s, both 3 H, –C$H_3$, isopropylidene), $^{13}$C NMR ($CDCl_3$) $\delta$ 204.77 (C=O), 173.36 (NH–C=O), 112.55 (isopropylidene), 99.50 (C-10), 84.37 (C-8), 73.97 (C-1), 70.95 (C-9), 66.23 (–$C$H$_2$–, C-12), 57.09 (C-2), 33.39 (–$C$H$_2$–, C-6), 29.96 (–$C$H$_2$–, C-5), 27.25, 26.79 (both –$C$H$_3$, isopropylidene). Anal. Calcd for $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05; N, 4.94. Found: C, 55.35; H, 6.18; N, 4.70.

*(1*R*,2*R*,9*S*,10*S*,11*R*) - 9,10 - Isopropylidene-dioxy - 12,14 - dioxa - 3 - aza - tricyclo[9.2.1.0$^{2,9}$]-tetradecan-4,8-dione* (**19**).—Application of Procedure D to the glutarimido derivative **15** (0.55 g, 1.86 mmol) for 8 h and subsequent column chromatography with 2:1–1:2 petroleum ether–EtOAc yielded recovered starting material (0.09 g, 16%) and compound **19** (0.40 g, 73%) as a white solid, which can be crystallised from 2-propanol to give colourless, prismatic crystals: mp 205–207 °C, $[\alpha]_D^{20}$ −143.6° (*c* 1.0, $CHCl_3$), $^1$H NMR ($CDCl_3$): $\delta$ 5.80 (d, 1 H, $J_{2,NH}$ 5.1 Hz, NH), 5.47 (d, 1 H, $J_{10,11}$ 3.1 Hz,H-11), 4.72 (d, 1 H, H-10), 4.55 (d, 1 H, $J_{1,13b}$ 6.3 Hz, H-1), 4.21 (dd, 1 H, H-13a), 4.13 (d, H-2), 3.83 (dd, 1 H, $J_{13a,13b}$ 7.5 Hz, H-13b), 3.38 (m, 1 H, H-7a), 2.52–2.42 (m, 2 H, H-5a, H-5b), 2.26 (m, 1 H, H-7b), 2.10–1.99 (m, 2 H, H-6a, H-6b), 1.61, 1.16 (both s, both 3 H, –C$H_3$, isopropylidene), $^{13}$C NMR ($CDCl_3$): $\delta$ 208.52 (C=O), 173.93 (NH–C=O), 112.41 (isopropylidene), 99.28 (C-11), 87.75 (C-9), 75.47 (C-1), 70.96 (C-10), 64.85 (–$C$H$_2$–, C-13), 53.01 (C-2), 36.46 (–$C$H$_2$–, C-7), 34.39 (–$C$H$_2$–, C-5), 27.97, 26.17 (both –$C$H$_3$, isopropylidene), 24.09 (–$C$H$_2$–, C-6). Anal. Calcd for $C_{14}H_{19}NO_6$: C, 56.56; H, 6.44; N, 4.71. Found: C, 56.56; H, 6.38; N, 4.71.

## 4. Supplementary material

Complete crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC no. 163492 (**19**), 163493 (**16**) and 163494 (**17**). Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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