cyclo{[(6-Amino-6-deoxy-2,3:4,5-di-O-isopropylidene-D-galactonic acid)-(D-Phe)]2}

Richard Bream,[a]***** David Watkin,**[a] **Raquel Soengas,**[b] **George W. J. Fleet,**[b] **Alison A. Edwards,**[c] **Stuart J. Hunter**[b] **and George E. Tranter**[c]

[a]Chemical Crystallography, Central Chemistry Laboratory, University of Oxford, Oxford OX1 3TA, England, [b]Department of Organic Chemistry, Chemical Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA, England, and [c]Biological Chemistry, Division of Biomedical Sciences, Imperial College, London SW7 2AZ, England

Correspondence e-mail:
richard.bream@pmb.ox.ac.uk

Determination of the crystal structure of the title compound [systematic name: 9,25-dibenzyl-4,4,15,15,20,20,31,31-octamethyl-3,5,14,16,19,21,30,32-octaoxa-8,11,24,27-tetraazapentacyclo[27.3.0.0^{2,6}.0^{13,17}.0^{18,22}]dotriacontane-7,10,23,26-tetrone], $C_{42}H_{56}N_4O_{12}$, a cyclic tetramer, established the relative stereochemistry of its ten stereogenic C atoms; an interesting saddle-like conformation is adopted. There are two molecules in the asymmetric unit. With the exception of the phenyl and isopropylidene groups, the molecules are related by a non-crystallographic twofold rotation axis. There are varying degrees of disorder in the isopropylidene groups.

Comment

Carbohydrates which contain amine and acid groups are commonly referred to as sugar amino acids (SAAs) (Chakraborty *et al.*, 2004; Gruner *et al.*, 2002; Smith & Fleet, 1999). They have been the focus of much interest as dipeptide isosteres and library scaffolds, and their linear oligomers as foldamers (Jensen & Brask, 2005, Trabocchi *et al.*, 2005). SAAs and α-amino acids have been combined in cyclic peptides (Stockle *et al.*, 2002; van Well *et al.*, 2000) to create mimics of biologically active cyclic peptides (van Well, Over-
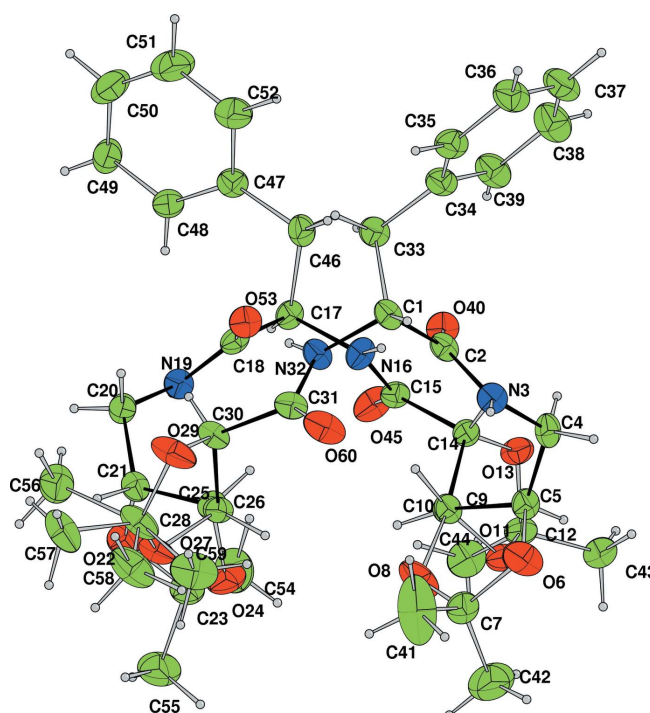

Figure 1
The title compound with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radii. The bonds in the 20-membered ring are black.

kleeft *et al.*, 2003; Gruner *et al.*, 2001). Several cyclic homo-oligomers have now been prepared using oxetane, furanose and pyranose SAAs (Johnson *et al.*, 2006; van Well, Marinelli *et al.*, 2003; Chakraborty *et al.*, 2003); a cyclic hexamer of pyranose SAAs was found to form inclusion complexes akin to those of cyclodextrins (Locardi *et al.*, 2001). A new family of cyclic SAA oligomers, based on acyclic SAAs, has been established (Mayes, Stetz *et al.*, 2004; Mayes, Simon *et al.*, 2004; Mayes, Cowley *et al.*, 2004) and a cyclic dimer of galactose stereochemistry found to interact with probe compounds (Edwards *et al.*, 2005). This family has now been expanded to include heterooligomers which incorporate phenylalanine (Phe).

The X-ray crystal structure confirms the structural integrity of the title compound, (3), and the absolute stereochemistry is determined by the use of D-galactonolactone as the starting material for the synthesis of (1). The saddle-like conformation adopted by (3) is of particular interest (Fig. 1).
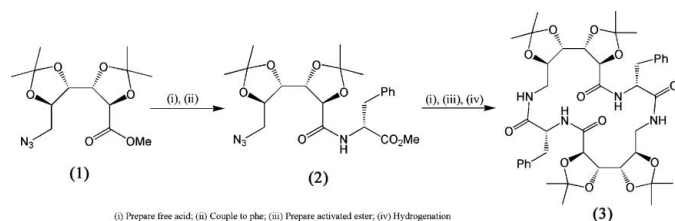
The material crystallizes in *P*1, with two molecules in the asymmetric unit (Fig. 2). The ring atoms in both molecules adopt the same conformation, the only differences being in the phenyl groups, which adopt different conformations in each molecule. The methyl groups on the isopropylidene rings show elongated displacement ellipsoids, and as such are probably disordered. Only two of the eight groups, one on each ring, are actually disordered enough to be modelled as such. The remaining groups were best modelled by large ADP. One of the isopropylidene rings also shows a disordered O atom, suggesting that it is the O atom on the ring, rather than the C atom with the methyl groups attached, that is flipping. Indeed, the dimethyl C atom has a small, well shaped displacement ellipsoid, suggesting that it does not move to any great degree, and the ring flips about it.

When the phenyl groups, the hydrogen and the isopropylidene methyl groups are removed, it is found that the skeletons of the two rings map on to each other, related by a pseudo-twofold rotation axis (r.m.s. deviation in atomic position = 0.137 Å; r.m.s. deviation in bond length = 0.012 Å; r.m.s. deviation in torsion angles = 5.78°).

The structure consists of ribbons of hydrogen-bonded molecules, with alternating inter- and intramolecular hydrogen bonds, parallel to the *a* axis (Table 1, and Figs. 3 and 4).

Experimental

Compound (3) was prepared by hydrogenation of the pentafluoro-phenyl ester of the linear SAA-Phe dimer (2) with palladized carbon
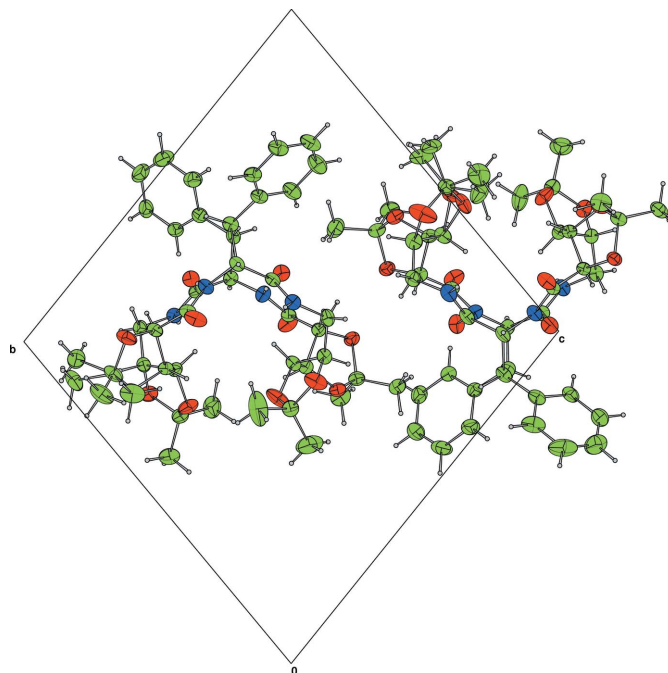

Figure 2
The asymmetric unit, viewed parallel to *a*, with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radii.
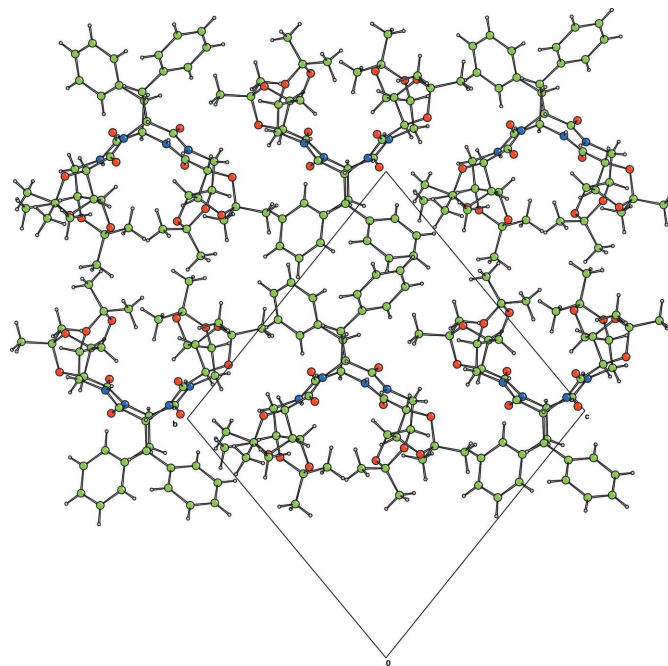

Figure 3
Packing diagram, viewed along the *a* axis, showing the hydrogen-bonded ribbons end on.

in dioxane; no cyclic dimer was observed. The linear dimer (2) was prepared by coupling of the free acid of SAA (1) (Long *et al.*, 1999) with the methyl ester of D-phenylalanine using standard peptide coupling reagents (*O*-benzotriazol-1-yl-*N*,*N*,*N*′,*N*′-tetramethyl-uronium tetrafluoroborate and triethylamine). The sample for X-ray analysis was crystallized from methanol.

The isopropylidene ring containing C144–C157 showed no deviation from equal occupancies, with the occupancies converging to 0.500 (3):0.500 (3). The H atoms were all located in a difference map, but those attached to C atoms were repositioned geometrically. The H atoms were initially refined with soft restraints on the bond lengths and angles to regularize their geometry (C—H in the range 0.93–0.98 Å, N—H in the range 0.86–0.89 Å and O—H = 0.82 Å) and displacement parameters [U_{iso}(H) in the range 1.2–1.5 times U_{eq} of the parent atom], after which they were refined with riding constraints.

Data collection: *COLLECT* (Nonius, 2001); cell refinement: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO/SCALEPACK*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *CAMERON* (Watkin *et al.*, 1996); software used to prepare material for publication: *CRYSTALS*.

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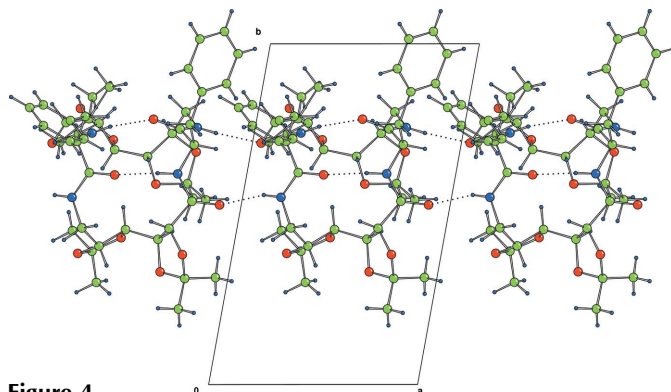
Figure 4
Packing diagram, viewed along the *c* axis, showing the hydrogen-bonded ribbons parallel to the *a* axis. Hydrogen bonds are drawn as dotted lines.

Crystal data

C$_{42}$H$_{56}$N$_4$O$_{12}$
$M_r = 808.93$
Triclinic, $P1$
$a = 9.1755$ (1) Å
$b = 15.4193$ (2) Å
$c = 15.5475$ (2) Å
$\alpha = 77.2624$ (5)°
$\beta = 82.0270$ (5)°
$\gamma = 78.2560$ (7)°

$V = 2090.45$ (4) Å^3
$Z = 2$
$D_x = 1.285$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.09$ mm^{-1}
$T = 150$ K
Needle, colourless
$0.60 \times 0.20 \times 0.20$ mm

Data collection

Nonius KappaCCD diffractometer
ω scans
Absorption correction: multi-scan
(*DENZO/SCALEPACK*;
Otwinowski & Minor, 1997)
$T_{min} = 0.621$, $T_{max} = 0.981$

17594 measured reflections
9415 independent reflections
9411 reflections with $I > -3\sigma(I)$
$R_{int} = 0.017$
$\theta_{max} = 27.5°$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.048$
$wR(F^2) = 0.089$
$S = 1.00$
9411 reflections
1090 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F^2) + (0.04P)^2 + 0.37P]$,
where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.47$ e Å^{-3}
$\Delta\rho_{min} = -0.26$ e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N119—H1$\cdots$O161	0.89	1.89	2.776 (2)	174
N16—H2$\cdots$O40	0.88	1.95	2.813 (2)	170
N116—H3$\cdots$O141^i	0.86	2.08	2.883 (2)	155
N132—H4$\cdots$O156^{ii}	0.85	2.09	2.916 (2)	163
N19—H5$\cdots$O60^{ii}	0.85	2.15	2.966 (2)	160
N3—H7$\cdots$O45^i	0.85	2.08	2.897 (2)	159
N32—H8$\cdots$O53	0.85	1.92	2.753 (2)	167
N102—H9$\cdots$O148	0.85	1.96	2.798 (2)	167

Symmetry codes: (i) $x - 1, y, z$; (ii) $x + 1, y, z$.

In the absence of significant anomalous scattering, Friedel pairs were merged. To model the disorder, those atoms with unusually elongated displacement ellipsoids were split, and each atom given an occupancy of 0.5. Coordinates, U^{ij} values and site occupancies of these atoms were then refined. No geometric restraints were applied. The isopropylidene ring containing C56–C59 showed significant deviation from equal occupancies, ending up at 0.581 (4):0.419 (4).