Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

(3*S*,2*R*)-3-Hydroxy-2-hydroxymethyl-7,9-diazaspiro[4.5]decane-6,8,10-trione

Marie-Thérèse Averbuch-Pouchot,[a] André Durif,[b]* Annabelle Renard,[b] Mitsuharu Kotera[b] and Jean Lhomme[b]

[a]LEDSS, UMR CNRS 5616, Université Joseph Fourier, BP 53, F-38041 Grenoble CEDEX 9, France, and [b]UMR CNRS 5616, Université Joseph Fourier, BP 53, F-38041 Grenoble CEDEX 9, France

Correspondence e-mail: andre.durif@ujf-grenoble.fr

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.002 Å
R factor = 0.039
wR factor = 0.044
Data-to-parameter ratio = 12.5

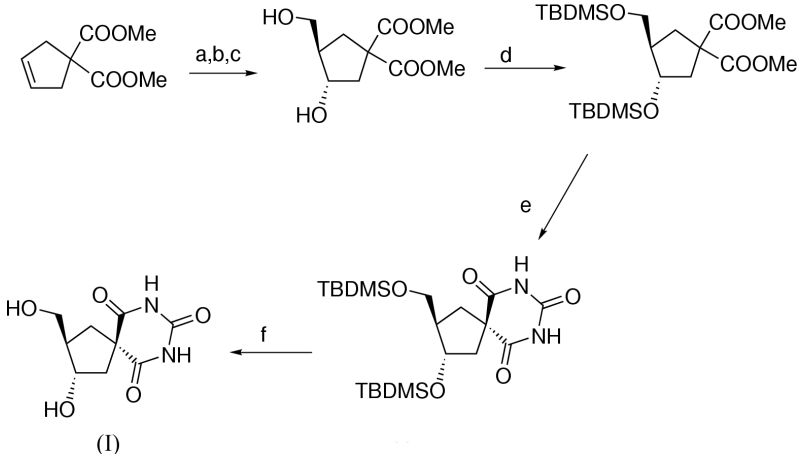
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The *trans* stereochemical relationship of the two substituents of the title compound, $C_9H_{12}N_2O_5$, a new spiro-nucleoside, has been confirmed. The cyclopentane moiety adopts the C3′-*endo*-type conformation, while the barbiturate ring is almost planar. Molecules interconnected by a two-dimensional network of hydrogen bonds build layers parallel to the *ab* plane.

Received 5 December 2001
Accepted 4 February 2002
Online 8 February 2002

Comment

Among many modified nucleosides exhibiting biological activities, some spiro-nucleosides have been shown to be useful as potent herbicides without animal toxicity. Synthetic efforts have been devoted in recent years to their analogues (Mio & Sano, 1997; Nakajima *et al.*, 1991). We are interested in the highly constrained structural feature of these spiro-nucleosides which may be used as promising building units for modified oligonucleotide synthesis in the antisense and/or the antigene strategy. It is well established that conformational restriction may lead to favourable complex formation due to an entropic advantage. This concept has been investigated quite intensively in nucleoside, and especially oligonucleotide, chemistry (Meldgaard & Wengel, 2000). Recently, we have developed synthetic methods for a new carbocyclic spiro-nucleoside containing the barbituric acid moiety, (I), using the synthetic scheme below (Renard *et al.*, 2002). The reagents and conditions are as follows: (*a*) $(CH_2O)_n$, AcOH, H_2SO_4, 333 K, 24 h; (*b*) trimethylsilyl choride (TMSCl), MeOH; (*c*) resolution; (*d*) *tert*-butyldimethylsilyl choride (TBDMSCl), imidazole; (*e*) urea, ^{t}BuOK; (*f*) TMSCl, MeOH; TBDMSO is *tert*-butyldimethylsilyl oxide.



(I)

We have shown that the spiro-nucleoside (I) is considerably more stable against ring opening than the deoxyribosyl deri-

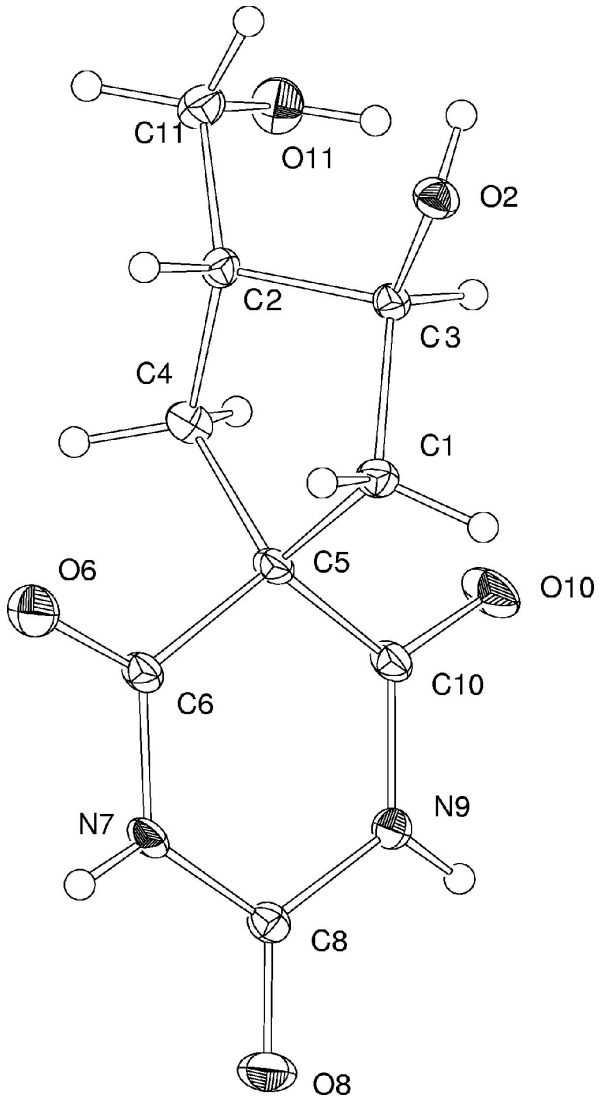


Figure 1
*ORTEP*II (Johnson, 1976) molecular diagram of the title compound. Ellipsoids are shown at the 25% probability level.

vative. Also, these compounds present enhanced hydrogen bonding capacity with the 'complementary' deoxyadenosine derivative. So it is interesting to determine the three-dimensional structure and hydrogen-bonding features of this spironucleoside.

The present atomic arrangement is a typical layer organization. Molecules of the title compound interconnected by N—H···O and O—H···O hydrogen bonds build up layers parallel to the *ab* plane. In this compound, as expected, the barbiturate ring is quasi-planar. The largest deviation from its least-squares plane is 0.102 (2) Å for C10. It is also worth noticing the relatively high density (1.623 Mg m^{-3}) of this compound.

Experimental

The title compound was prepared according to the process described by Renard *et al.* (2002). To a solution of 3′,5′-*O*-bis(*tert*-butyldimethylsilyl)spirocyclopentylbarbituric acid (2.0 g, 4.4 mmol) in MeOH (10 ml) was added TMSCl (500 µl). This solution was stirred at room temperature for 15 min while the deprotected spirocyclopentylbarbituric acid precipitated in the medium. The volatile material was removed under reduced pressure and the resulting residue was triturated into Et_2O to afford a white powder (1.0 g, 4.3 mmol, 99%; m.p. 487–489 K). TLC (MeOH/CH_2Cl_2 20:80): R_f 0.28. $[\alpha]_D^{25}$ = +34.8 (c = 0.91, MeOH). IR (KBr): ν 3351, 3197, 3076, 2844, 1754, 1740, 1689, 1444, 1352, 1175, 1081, 807 cm^{-1}. ^{1}H NMR (200 MHz, [D_6]DMSO): δ 1.65–2.30 (*m*, 5H, H-2′, H-4′, H-6′), 3.31 (*m*, 1H, H-5′), 3.56 (*m*, 1H, H-5′), 3.82 (*m*, 1H, H-3′), 4.42 (*m*, OH-5′), 4.84 (*m*, OH-3′), 11.0 (*br s*, 2H, NH). ^{13}C NMR (50 MHz, [D_6]DMSO): δ = 37.9 (C-6′), 42.5 (C-2′),49.0 (C-4′), 51.9 (C-1′), 61.3 (C-5′), 72.5 (C-3′), 150.5 (C═O), 174.6 (C═O). MS (FAB-, glycerol): *m*/*z*: 227 [*M*—H]. Analysis for $C_9H_{12}N_2O_5$ (228.20), calculated: C 47.37, H 5.30, N 12.28%; found: C 47.46, H 5.46, N 12.27%. Crystals were obtained by slow evaporation of a solution in water.

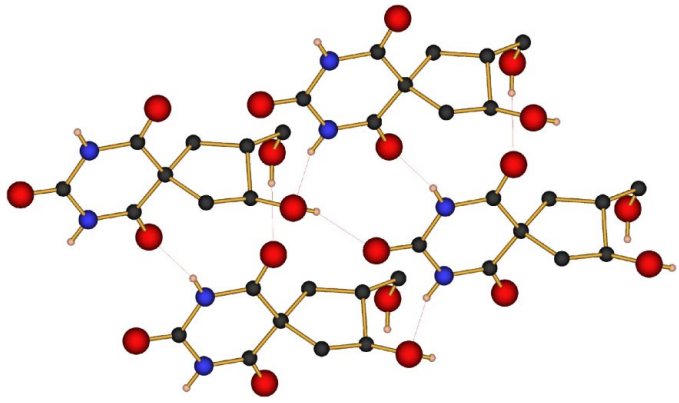


Figure 2
The two-dimensional hydrogen-bond network projected along the *c* axis. Black circles represent C atoms, blue circles N atoms, red circles O atoms, and small circles H atoms. Hydrogen bonds are depicted by dotted lines.

Crystal data

$C_9H_{12}N_2O_5$
M_r = 228.20
Monoclinic, $P2_1$
a = 7.467 (2) Å
b = 6.802 (1) Å
c = 9.673 (3) Å
β = 108.07 (2)°
V = 467.1 (2) Å^3
Z = 2
D_x = 1.623 Mg m^{-3}
Mo Kα radiation
Cell parameters from 25 reflections
θ = 9.3–12.7°
μ = 0.13 mm^{-1}
T = 293 K
Monoclinic prism, colourless
0.32 × 0.16 × 0.09 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
ω scans
Absorption correction: none
2284 measured reflections
2187 independent reflections
1818 reflections with $I > 1.5\sigma(I)$
R_{int} = 0.014
θ_{max} = 35°
$h = -12 \rightarrow 12$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 15$
2 standard reflections
frequency: 120 min
intensity decay: 0.2%

Refinement

Refinement on F
R = 0.039
wR = 0.044
S = 1.40
1817 reflections
145 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F_o) + 0.00006|F_o|^2]$
$(\Delta/\sigma)_{max}$ = 0.004
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O2—C2	1.425 (2)	C1—C2	1.519 (2)
O6—C6	1.217 (2)	C1—C5	1.566 (2)
O8—C8	1.219 (2)	C2—C3	1.532 (2)
O10—C10	1.218 (2)	C3—C4	1.523 (2)
O11—C11	1.417 (2)	C3—C11	1.523 (2)
N7—C6	1.359 (2)	C4—C5	1.563 (2)
N7—C8	1.371 (2)	C5—C6	1.511 (2)
N9—C8	1.372 (2)	C5—C10	1.503 (2)
N9—C10	1.365 (2)		
C6—N7—C8	126.0 (1)	C4—C5—C6	109.1 (1)
C8—N9—C10	125.4 (1)	C4—C5—C10	111.9 (1)
C2—C1—C5	104.2 (1)	C6—C5—C10	113.5 (1)
O2—C2—C1	109.5 (1)	O6—C6—N7	120.4 (1)
O2—C2—C3	114.6 (1)	O6—C6—C5	120.7 (1)
C1—C2—C3	102.7 (1)	N7—C6—C5	118.8 (1)
C2—C3—C4	102.2 (1)	O8—C8—N7	121.9 (1)
C2—C3—C11	115.9 (1)	O8—C8—N9	122.0 (1)
C4—C3—C11	115.0 (1)	N7—C8—N9	116.0 (1)
C3—C4—C5	105.7 (1)	O10—C10—N9	119.5 (1)
C1—C5—C4	104.5 (1)	O10—C10—C5	122.1 (1)
C1—C5—C6	109.9 (1)	N9—C10—C5	118.3 (1)
C1—C5—C10	107.6 (1)	O11—C11—C3	114.0 (1)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O11—H12···O6^{i}	0.81	2.00	2.809 (2)	173
N7—H8···O10^{ii}	0.86	1.99	2.840 (2)	170
N9—H9···O2^{iii}	0.85	2.04	2.862 (1)	161

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

The H atoms attached to C were positioned geometrically whereas H atoms on O or N were located from a difference Fourier map; in both cases, they were not refined. Since there is a twofold screw axis, in order to avoid any remaining shifts, we chose to constrain, as origin, the atom O2, by fixing its *y* coordinate instead of fixing the sum of coordinates. Because of the lack of any significant anomalous dispersion effects, the absolute configuration could not be determined from the diffraction experiment. Friedel pairs in the data set were merged prior to refinement.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1992–1997); program(s) used to solve structure: *SIR* 92 (Altomare *et al.*, 1994); program(s) used to refine structure: *TEXSAN*; software used to prepare material for publication: *TEXSAN*.

References

Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.

Enraf–Nonius (1989). *CAD*-4 *Sofware*. Enraf–Nonius, Delft, The Netherlands.

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Meldgaard, M. & Wengel, J. (2000). *J. Chem. Soc. Perkin Trans.* 1, pp. 3539–3554.

Mio, S. & Sano, H. (1997). *Annu. Rep. Sankyo Res. Lab.* **49**, 91–119.

Molecular Structure Corporation (1992–1997). *TEXSAN*. Version 1.7. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.

Nakajima, M., Itoi, K., Takamatsu, Y., Kinoshita, T., Okazaki, T., Kawakubo, K., Shindo, M., Honma, T., Tohjigamori, M. & Haneishi, T. (1991). *J. Antibiot.* **44**, 293–300.

Renard, A., Kotera, M. & Lhomme, J. (2002). *J.. Org. Chem.* In the press.