Acta Crystallographica Section C
**Crystal Structure Communications**
ISSN 0108-2701

# Regioisomeric 4-nitroindazole $N^1$- and $N^2$-($\beta$-D-ribonucleosides)

**Frank Seela,[a]* Xiaohua Peng,[a] Henning Eickmeier[b] and Hans Reuter[b]**

[a]Laboratorium für Organische und Bioorganische Chemie, Institut für Chemie, Universität Osnabrück, Barbarastraße 7, 49069 Osnabrück, Germany, and [b]Anorganische Chemie II, Institut für Chemie, Universität Osnabrück, Barbarastraße 7, 49069 Osnabrück, Germany
Correspondence e-mail: frank.seela@uni-osnabrueck.de

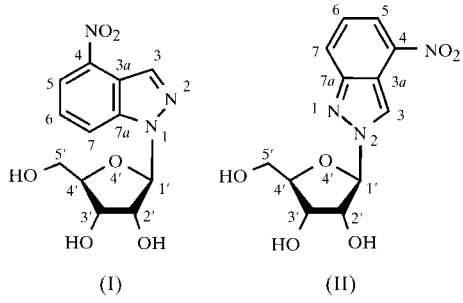
Received 2 October 2003
Accepted 18 November 2003
Online 20 December 2003

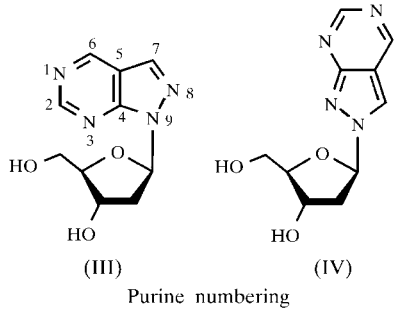
The structures of the isomeric nucleosides 4-nitro-1-($\beta$-D-ribofuranosyl)-1*H*-indazole, $C_{12}H_{13}N_3O_6$, (I), and 4-nitro-2-($\beta$-D-ribofuranosyl)-2*H*-indazole, $C_{12}H_{13}N_3O_6$, (II), have been determined. For compound (I), the conformation of the glycosylic bond is *anti* [$\chi$ = −93.6 (6)°] and the sugar puckering is C2′-*exo*–C3′-*endo*. Compound (II) shows two conformations in the crystalline state which differ mainly in the sugar pucker; type 1 adopts the C2′-*endo*–C3′-*exo* sugar puckering associated with a *syn* base orientation [$\chi$ = 43.7 (6)°] and type 2 shows C2′-*exo*–C3′-*endo* sugar puckering accompanied by a somewhat different *syn* base orientation [$\chi$ = 13.8 (6)°].

## Comment

Universal nucleosides, which base-pair equally well with the canonical four nucleic acid constituents, either ribonucleosides or 2′-deoxyribonucleosides, are categorized into two types, namely those forming base pairs by hydrogen-bonding and those whose stability depends mainly on stacking interactions. 5-Nitro-1*H*-indole 2′-deoxy-$\beta$-D-ribofuranoside, which has been incorporated in duplex DNA, shows such universal base-pairing properties. It belongs to the second category of universal nucleosides, which stabilize DNA by stacking interactions rather than by hydrogen bonding (Loakes & Brown, 1994). Likewise, the regiosiomeric 4-nitroindazole 2′-deoxyribonucleosides have been shown to act as universal nucleosides because they behave indiscriminately towards the four natural DNA constituents (Seela & Bourgeois, 1991; Seela & Jawalekar, 2002). Recently, the title regioisomeric 4-nitroindazole $N^1$- and $N^2$-($\beta$-D-ribonucleosides), (I) and (II), have been prepared (Seela & Peng, 2004; Revankar & Townsend, 1970). Here, the single-crystal structure analyses of (I) and (II) are described.

For the canonical ribonucleosides, the orientation of the base relative to the sugar (*syn*/*anti*) is defined by the torsion angle $\chi$ (O4′—C1′—N9—C4) (purine numbering; IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983). The preferred conformation at the N-glycosylic bond of the common purine nucleosides is usually *anti* (Saenger, 1989). By analogy, the torsion angle $\chi$ of compound (I) is here defined as O4′—C1′—N1—C7a. For compound (II), the analogy is less straightforward, but the torsion angle related to $\chi$ is defined as O4′—C1′—N2—C3, as in the corresponding pyrazolo[3,4-*d*]-pyrimidine (Seela & Debelak, 2000). The C2′-*endo* (*S*) and C3′-*endo* (*N*) puckerings are the most frequently observed sugar-ring conformations of nucleosides (Saenger, 1984*a*). Among these, ribonucleosides often show C3′-*endo* sugar puckering with a half-chair or envelope conformation.




The structure of (I) is shown in Fig. 1 and selected geometric parameters are summarized in Table 1 (systematic numbering is used throughout). For (I), the conformation of the glycosylic bond is between the *anti* and the high-*anti* range [$\chi$ = −93.6 (6)°], which was also observed for 1-(2-deoxy-$\beta$-D-erythropentofuranosyl)-4-nitro-1*H*-indazole [$\chi$ = −105.2 (5)°; Seela & Jawalekar, 2003], 2-(2′-deoxy-$\beta$-D-erythropentofuranosyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine, (III) [$\chi$ = −100.4 (2)°; He *et al.*, 2002] and pyrazolo[3,4-*d*]pyrimidine-4-amine 2′-deoxyribonucleoside [8-aza-7-deaza-2′-deoxyadenosine; $\chi$ = −106.3 (2)°; Seela *et al.*, 1999]. The puckering of the ribose ring in (I) is C2′-*exo*–C3′-*endo*, showing an *N*-type sugar conformation ($^3T_2$) with pseudorotation parameters (Saenger, 1984*b*) of $P$ = 6.5 (4)° and $\tau_m$ = 38.3°. The torsion angle $\gamma$ (O5′—C5′—C4′—C3′) is 58.0 (7)°, which corresponds to +*sc* (Saenger, 1984*b*). In contrast, 4-nitro-1*H*-indazole 2′-deoxyribonucleoside displays *S*-type sugar puckering and the orientation of the exocyclic C4′—C5′ bond is −*sc* (Seela & Jawalekar, 2003).

The base moiety of nucleoside (I) is nearly planar; the r.m.s. deviation of the ring atoms (N1/N2/C3–C7/C7a/C3a) from

  DOI: 10.1107/S0108270103026556 

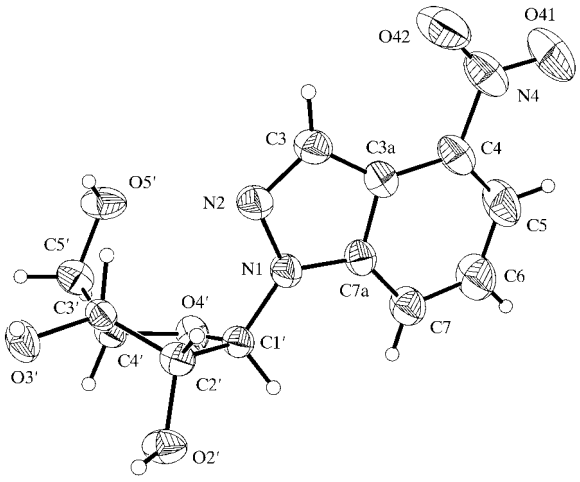



**Figure 1**
A perspective view of nucleoside (I) showing the atomic numbering. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

their calculated least-squares planes is 0.0218 Å, with a maximum deviation of 0.037 (4) Å for atom N1. However, the exocyclic substituents (nitro atom N4 and atom C1′) show significant deviations from the plane [0.14 (1) and 0.052 (9) Å, respectively] and lie on the same side of the base.

The bases are strongly stacked in the crystal structure of (I). There are three intermolecular hydrogen bonds responsible for the packing of the molecules (Table 2). The O5′—H5′*A*···O2′($x-1$, $y$, $z$) bond connects molecules parallel to the *a* axis, forming infinite chains in which the bases are stacked and parallel to each other (Fig. 2). Another two interchain hydrogen bonds, *viz.* O3′—H3′*A*···O5′($1-x$, $\frac{1}{2}+y$, $1-z$) and O2′—H2′*A*···O4′($2-x$, $\frac{1}{2}+y$, $1-z$), are found linking two neighbouring chains.

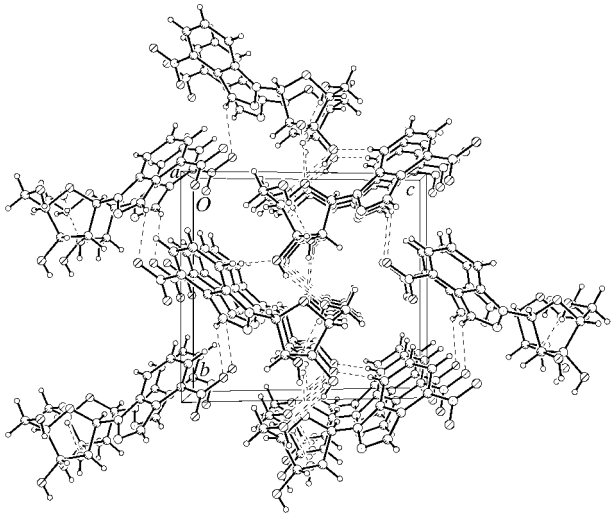



**Figure 2**
The crystal packing in (I), viewed down the *a* axis, showing the intermolecular hydrogen bonding.

Compound (II) differs from compound (I) only in the glycosylation position (N2 *versus* N1), yet it shows a significantly different structure in the crystalline state (Fig. 3). Slow crystallization of 4-nitro-2*H*-indazole $N^2$-ribonucleoside from methanol gave crystals which consist of two forms of molecules, defined as types 1 and 2, denoted (II-1) and (II-2), respectively, while nucleoside (I) displays only one structure. A comparison of these two different structures shows that both exhibit a *syn* conformation of the N-glycosylic bond, with different torsion angles: $\chi$ = 43.7 (6) for (II-1) and 13.8 (6)° for (II-2). 2-(2-Deoxy-$\beta$-D-erythropentofuranosyl)-2*H*-pyrazolo[3,4-*d*]pyrimidine, (IV), shows similar values (He *et al.*, 2002). The structures of nucleosides (II-1) and (II-2) are shown in Fig. 3.

The structures of (II-1) and (II-2) differ mainly in the sugar ring conformations (Table 3). For (II-2), the sugar shows *N*-

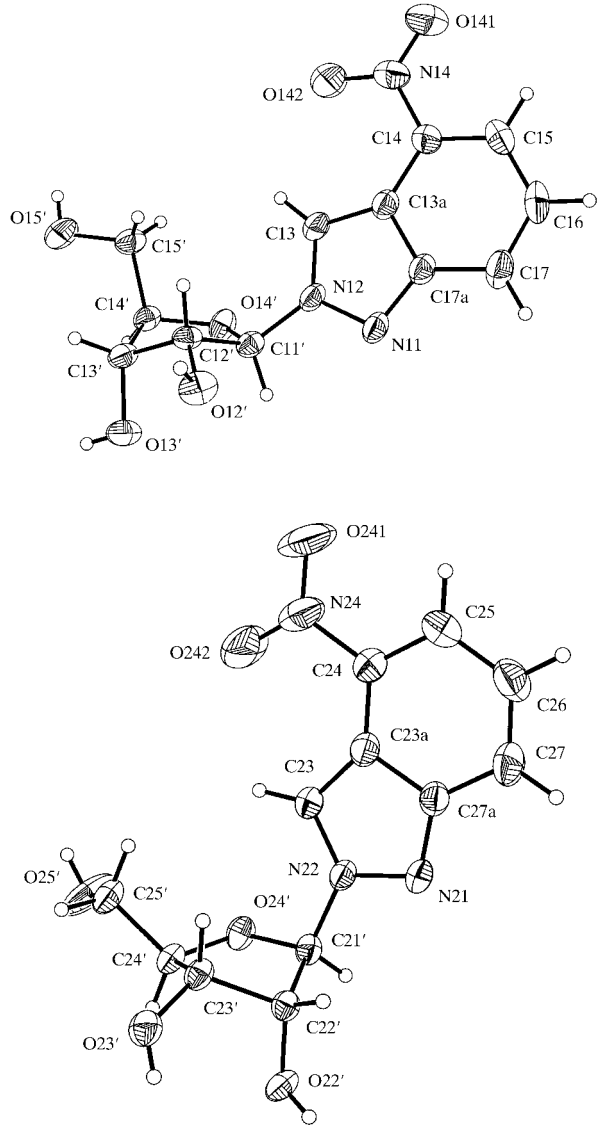



**Figure 3**
Perspective views of (*a*) molecule (II-1) and (*b*) molecule (II-2). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

type sugar puckering ($P$ = 2.1°, C2′-*exo*–C3′-*endo*, $^3T_2$) with a puckering amplitude $\tau_m$ = 41.1°, a value which is very close to that of (I), whereas *S*-type sugar puckering ($P$ = 185.4°, C2′-*endo*–C3′-*exo*, $_3T^2$, $\tau_m$ = 40.6°) characterizes (II-1) (Saenger, 1984*b*). Both (II-1) and (II-2) display different conformations about the C4′—C5′ bond; the former is −*sc* (−*gauche*) (Saenger, 1984*b*) with a torsion angle $\gamma$ (O5′—C5′—C4′—C3′) of −80.9 (5)°, whereas the latter is −*ap* (*trans*) (Saenger, 1984*b*) with $\gamma$ = −176.1 (5)°.

The base moieties of compound (II) are nearly planar, showing maximum deviations of their C and N atoms from the least-squares plane ranging from −0.007 (4) to 0.005 (4) Å for (II-1) and from −0.008 (4) to 0.007 (3) Å for (II-2). The structure of nucleoside (II) is stabilized by several intermolecular hydrogen bonds between conformations (II-1) and (II-2) (Table 4 and Fig. 4), leading to the formation of layers. In every layer, each molecule links two neighbouring molecules of different conformations through four intermolecular hydrogen bonds, *viz.* O12′—H12*A*···O22′($x$, $y-1$, $z-1$), O13′—H13O···O23′($x-1$, $y-1$, $z$), O22′—H22*A*···O13′-($1+x$, $1+y$, $1+z$) and O23′—H23O···O15′($x$, $1+y$, $z$). Two further hydrogen bonds between the sugar moieties and the adjacent nucleobase units are found linking molecules of identical conformation [O15′—H15*A*···N11($1+x$, $y$, $1+z$) for (II-1) and O25′—H25*A*···N21($x-1$, $y$, $z-1$) for (II-2)].

Compounds (I) and (II) show different sugar conformations in the solid state: nucleoside (I) shows only the *N* conformation, but compound (II) displays two conformations, *N* and S. In solution, both regioisomers are observed to be a mixture of *N*- and *S*-conformers. The populations of *N*- and *S*-conformers in $D_2O$ solution were found to be 53% *N* and 47% *S* for nucleoside (I), and 51% *N* and 49% S for (II). This was shown by $^1$H NMR spectroscopy using the vicinal [$^1$H,$^1$H] coupling constants and applying the *PSEUROT* program (Van Wijk *et al.*, 1999).

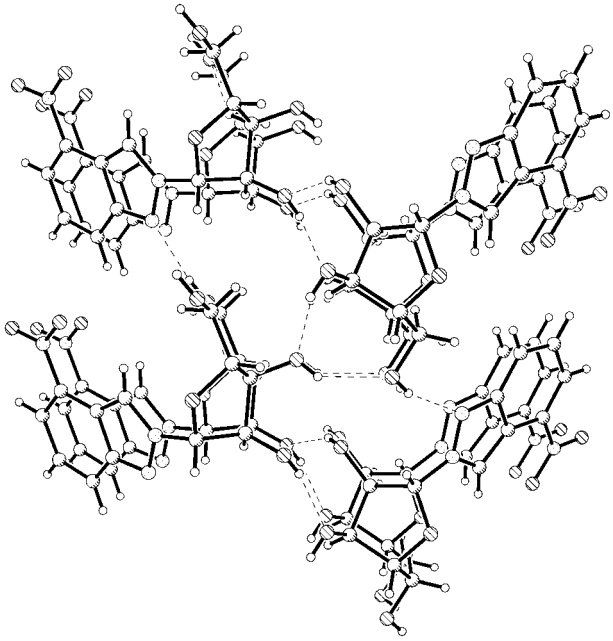


**Figure 4**
The hydrogen bonding within the double layers of the crystal structure of (II).

## Experimental

The syntheses of compounds (I) and (II) have been published elsewhere (Seela & Peng, 2004). Both compounds were crystallized slowly from MeOH.

### Compound (I)

*Crystal data*

$C_{12}H_{13}N_3O_6$
$M_r$ = 295.25
Monoclinic, $P2_1$
$a$ = 5.8912 (11) Å
$b$ = 10.0825 (12) Å
$c$ = 11.0998 (17) Å
$\beta$ = 102.821 (15)°
$V$ = 642.87 (17) Å$^3$
$Z$ = 2
$D_x$ = 1.525 Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 30 reflections
$\theta$ = 6.1–12.5°
$\mu$ = 0.12 mm$^{-1}$
$T$ = 293 (2) K
Block, yellow
0.6 × 0.4 × 0.3 mm

*Data collection*

Bruker *P*4 diffractometer
$2\theta/\omega$ scans
2712 measured reflections
1960 independent reflections
1659 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.043
$\theta_{max}$ = 30.0°
$h = -8 \rightarrow 1$
$k = -1 \rightarrow 14$
$l = -15 \rightarrow 15$
3 standard reflections
every 97 reflections
intensity decay: none

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.126
$S$ = 1.05
1960 reflections
199 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0654P)^2 + 0.0968P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.30 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.28 e Å$^{-3}$

**Table 1**
Selected geometric parameters (Å, °) for (I).

| | | | |
|---|---|---|---|
| N1—C1′ | 1.450 (6) | | |
| N2—N1—C1′ | 120.6 (4) | C7a—N1—C1′ | 127.9 (5) |
| C1′—N1—N2—C3 | −179.0 (5) | N1—C1′—O4′—C4′ | −114.4 (5) |
| N2—N1—C1′—O4′ | 83.5 (6) | C1′—O4′—C4′—C5′ | 141.4 (5) |
| C7a—N1—C1′—O4′ | −93.6 (6) | C1′—O4′—C4′—C3′ | 16.5 (5) |
| C7a—N1—C1′—C2′ | 147.7 (5) | C2′—C3′—C4′—O4′ | −33.8 (5) |
| O4′—C1′—C2′—C3′ | −28.9 (5) | O3′—C3′—C4′—C5′ | 82.4 (6) |
| N1—C1′—C2′—C3′ | 92.4 (5) | O4′—C4′—C5′—O5′ | −59.5 (7) |
| C1′—C2′—C3′—O3′ | 158.4 (4) | C3′—C4′—C5′—O5′ | 58.0 (7) |
| C1′—C2′—C3′—C4′ | 37.8 (5) | | |

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O2′—H2′*A*···O4′$^{i}$ | 0.84 (12) | 1.96 (12) | 2.800 (6) | 173 (9) |
| O3′—H3′*A*···O5′$^{ii}$ | 0.80 (12) | 2.09 (11) | 2.832 (7) | 154 (10) |
| O5′—H5′*A*···O2′$^{iii}$ | 0.82 (4) | 1.97 (5) | 2.784 (7) | 168 (10) |

Symmetry codes: (i) $2-x, \frac{1}{2}+y, 1-z$; (ii) $1-x, \frac{1}{2}+y, 1-z$; (iii) $x-1, y, z$.

## Compound (II)

*Crystal data*

$C_{12}H_{13}N_3O_6$
$M_r$ = 295.25
Monoclinic, $P2_1$
$a$ = 4.9355 (13) Å
$b$ = 35.936 (5) Å
$c$ = 7.1833 (9) Å
$\beta$ = 99.311 (18)°
$V$ = 1257.2 (4) Å$^3$
$Z$ = 4
$D_x$ = 1.560 Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 44 reflections
$\theta$ = 4.5–12.4°
$\mu$ = 0.13 mm$^{-1}$
$T$ = 293 (2) K
Block, yellow
0.4 × 0.3 × 0.2 mm

*Data collection*

Bruker $P4$ diffractometer
$2\theta/\omega$ scans
4996 measured reflections
3706 independent reflections
2657 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.048
$\theta_{max}$ = 30.0°
$h = -1 \rightarrow 6$
$k = -1 \rightarrow 50$
$l = -10 \rightarrow 10$
3 standard reflections
every 97 reflections
intensity decay: none

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.061
$wR(F^2)$ = 0.170
$S$ = 1.04
3706 reflections
397 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0767P)^2 + 0.5939P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.30 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.36 e Å$^{-3}$

**Table 3**
Selected geometric parameters (Å, °) for (II).

| | | | |
|---|---|---|---|
| N12—C11′ | 1.463 (6) | N22—C21′ | 1.470 (6) |
| C13—N12—C11′ | 127.3 (4) | C23—N22—C21′ | 128.8 (4) |
| N11—N12—C11′ | 118.5 (4) | N21—N22—C21′ | 117.8 (3) |
| C13—C13a—C17a—C17 | 179.2 (5) | C23—N22—C21′—O24′ | 13.8 (6) |
| C13—N12—C11′—O14′ | 43.7 (6) | N21—N22—C21′—O24′ | −169.6 (4) |
| N11—N12—C11′—O14′ | −137.0 (4) | N21—N22—C21′—C22′ | 72.7 (5) |
| N11—N12—C11′—C12′ | 104.3 (4) | O24′—C21′—C22′—C23′ | −32.6 (4) |
| O14′—C11′—C12′—C13′ | 30.9 (4) | N22—C21′—C22′—C23′ | 86.3 (4) |
| N12—C11′—C12′—C13′ | 150.8 (3) | C21′—C22′—C23′—O23′ | 164.1 (3) |
| C11′—C12′—C13′—O13′ | 76.8 (4) | C21′—C22′—C23′—C24′ | 40.1 (4) |
| C11′—C12′—C13′—C14′ | −39.6 (4) | C22′—C21′—O24′—C24′ | 11.8 (4) |
| C12′—C11′—O14′—C14′ | −9.3 (4) | C21′—O24′—C24′—C23′ | 14.5 (4) |
| C12′—C13′—C14′—O14′ | 35.2 (4) | C22′—C23′—C24′—O24′ | −34.5 (4) |
| O14′—C14′—C15′—O15′ | 162.8 (4) | O23′—C23′—C24′—C25′ | 81.0 (5) |
| C13′—C14′—C15′—O15′ | −80.9 (5) | O24′—C24′—C25′—O25′ | 67.8 (5) |
| C23—C23a—C27a—C27 | −179.8 (5) | C23′—C24′—C25′—O25′ | −176.1 (5) |

**Table 4**
Hydrogen-bonding geometry (Å, °) for (II).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O12′—H12$A$···O22′$^{i}$ | 0.82 (5) | 2.08 (3) | 2.841 (5) | 154 (6) |
| O13′—H13O···O23′$^{ii}$ | 0.83 (7) | 1.96 (3) | 2.720 (4) | 154 (6) |
| O15′—H15$A$···N11$^{iii}$ | 0.82 (5) | 2.14 (4) | 2.928 (6) | 162 (2) |
| O22′—H22$A$···O13′$^{iv}$ | 0.82 (2) | 1.95 (5) | 2.741 (4) | 161 (6) |
| O23′—H23O···O15′$^{v}$ | 0.82 (2) | 2.14 (2) | 2.839 (6) | 144 (3) |
| O25′—H25$A$···N21$^{vi}$ | 0.83 (7) | 1.99 (7) | 2.812 (5) | 172 (2) |

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

The known configuration of the sugar moiety was used to define the enantiomer employed in the refined model. All H atoms were initially found in a difference Fourier synthesis. In order to maximize the data-to-parameter ratio, H atoms bonded to C atoms were placed in geometrically idealized positions (C—H = 0.93–0.98 Å) and constrained to ride on their parent atoms, with $U_{iso}$(H) = 1.2$U_{eq}$(C).

For both compounds, data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Sheldrick, 1997); program(s) used to solve structure: *SHELXTL*; program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 1999).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1127). Services for accessing these data are described at the back of the journal.

## References

He, J.-L., Seela, F., Eickmeier, H. & Reuter, H. (2002). *Acta Cryst.* C**58**, o593–o595.
IUPAC–IUB Joint Commission on Biochemical Nomenclature (1983). *Eur. J. Biochem.* **131**, 9–15.
Loakes, D. & Brown, D. M. (1994). *Nucleic Acids Res.* **20**, 4039–4043.
Revankar, G. R. & Townsend, L. B. (1970). *J. Heterocycl. Chem.* **7**, 117–121.
Saenger, W. (1984*a*). *Principles of Nucleic Acid Structure*, edited by C. R. Cantor, pp. 55–61. New York: Springer–Verlag.
Saenger, W. (1984*b*). *Principles of Nucleic Acid Structure*, edited by C. R. Cantor, pp. 14–20. New York: Springer–Verlag.
Saenger, W. (1989). *Landolt–Börnstein New Series*, Vol. 1, *Nucleic Acids*. subvolume a, edited by O. Madelung, pp. 1–21. Berlin: Springer–Verlag.
Seela, F. & Bourgeois, W. (1991). *Helv. Chim. Acta*, **74**, 315–322.
Seela, F. & Debelak, H. (2000). *Nucleic Acids Res.* **28**, 3224–3232.
Seela, F. & Jawalekar, A. (2002). *Helv. Chim. Acta*, **85**, 1857–1868.
Seela, F. & Jawalekar, A. (2003). Unpublished results.
Seela, F. & Peng, X. H. (2004). *Nucleosides Nucleotides Nucleic Acids*, **23**, 227–237.
Seela, F., Zulauf, M., Reuter, H. & Kastner, G. (1999). *Acta Cryst.* C**55**, 1947–1950.
Sheldrick, G. M. (1997). *SHELXTL*. Release 5.10. Bruker AXS Inc., Madison, Wisconsin, USA.
Siemens (1996). *XSCANS*. Release 2.2. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Spek, A. L. (1999). *PLATON for Windows*. University of Utrecht, The Netherlands. (32-Bit Windows Implentation by L. J. Farrugia, University of Glasgow, Scotland.)
Van Wijk, L., Haasnoot, C. A. G., de Leeuw, F. A. A. M., Huckriede, B. D., Westra Hoekzema, A. J. A. & Altona, C. (1999). *PSEUROT*. Version 6.3. Leiden Institute of Chemistry, Leiden University, The Netherlands.