

The Structure of a Uridine Derivative in the *syn* Conformation: 6,7-Dimethyl-*N*-1- β -D-ribofuranosyllumazine

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6,7-Dimethyl-*N*-1- β -D-ribofuranosyllumazine (I), $C_{13}H_{16}N_4O_6$, is monoclinic, space group $P2_1$, with $a = 6.909$ (2), $b = 19.093$ (4), $c = 10.806$ (2) Å, $\beta = 96.65$ (3)°, $Z = 4$. The structure was determined by direct methods from 4286 diffractometer-measured X-ray data (Cu $K\alpha$, Ni filter) and refined to $R = 5.9\%$. (I) is in the *syn* conformation which is stabilized by an intramolecular O(5')–H...O(2) hydrogen bond; the sugar is C(2')-*endo* puckered; the orientation about C(4')–C(5') is *gauche, gauche*. The heterocycles are folded by about 5° and stacked 3.45 Å apart along a ; the riboses are connected by hydrogen bonds.

Introduction

The pteridine nucleoside 6,7-dimethyl-*N*-1- β -D-ribofuranosyllumazine (I, Fig. 1) was obtained by chemical synthesis (Ritzmann, Harzer & Pfeleiderer, 1971). It can be considered as an analogue of uridine with the heterocycle augmented by a pyrazine ring system. As substitution in position 6 of the uracil ring usually leads to uridine derivatives in the *syn* conformation (Suck & Saenger, 1972) it was of interest to study (I) more closely. So far only a few pyrimidine nucleosides have

been observed in this conformation, namely cytidine-2',3'-cyclophosphate (Coulter, 1973), 4-thiouridine (Saenger & Scheit, 1970), 3',5'-diacetyl-2'-deoxy-2'-fluorouridine (Suck, Saenger, Main, Germain & Declercq, 1974), 6-methyluridine (Suck & Saenger, 1972). In this paper the structure of (I) is reported. A preliminary account has been given (Saenger, Ritzmann & Pfeleiderer, 1972).

Experimental

(I) crystallized from aqueous solution as thick plates. Although the crystals show twinning with b^*c^* as twin plane, a single crystal could be cut. Crystallographic data were determined by photographic and diffractometer methods and are summarized in Table 1.

4286 intensities were collected on a Stoe four-circle diffractometer equipped with a Mo tube and graphite monochromator ($\lambda = 0.70926$ Å). The data were corrected for monochromator polarization effects ($\theta =$

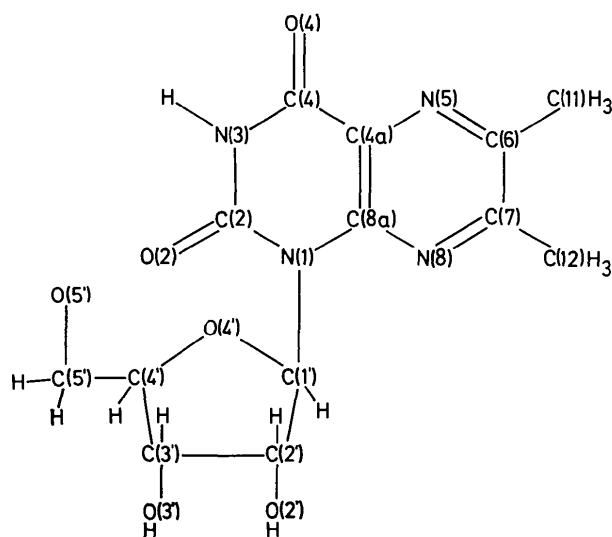


Fig. 1. Chemical formula and numbering scheme for 6,7-dimethyl-*N*-1- β -D-ribofuranosyllumazine.

Table 1. Crystallographic data

$C_{13}H_{16}N_4O_6$, $M_r = 324.3$
Monoclinic, space group $P2_1$
$a = 6.909$ (2) Å
$b = 19.093$ (3)
$c = 10.806$ (2)
$\beta = 96.65$ (3)°
$V_c = 1415.9$ Å ³
$D_c = 1.522$ g cm ⁻³
$Z = 4$
Size of crystal: 0.2 × 0.3 × 0.5 mm
Data measured: 4286
Radiation used: Mo $K\alpha$, $\lambda = 0.70926$ Å
Graphite monochromator, $\theta = 6^\circ$
$R = \sum F_o - F_c / \sum F_o = 5.9\%$

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Table 2. *Fractional atomic coordinates* ($\times 10^4$)

Standard deviations were determined from the least-squares correlation matrix and average 0.0004, 0.0001 and 0.0002 for x , y and z respectively.

	x	y	z
C(1') <i>A</i>	3934	2048	-5874
C(2') <i>A</i>	5245	1511	-6434
O(2') <i>A</i>	7239	1656	-6197
C(3') <i>A</i>	4390	1548	-7809
O(3') <i>A</i>	5243	2144	-8305
C(4') <i>A</i>	2214	1653	-7744
O(4') <i>A</i>	2049	1972	-6533
C(5') <i>A</i>	971	998	-7857
O(5') <i>A</i>	1696	452	-7019
N(1) <i>A</i>	3763	2003	-4536
C(2) <i>A</i>	3374	1372	-3995
O(2) <i>A</i>	3092	828	-4574
N(3) <i>A</i>	3344	1376	-2719
C(4) <i>A</i>	3457	1938	-1924
O(4) <i>A</i>	3338	1862	-814
C(4a) <i>A</i>	3661	2608	-2556
N(5) <i>A</i>	3681	3205	-1887
C(6) <i>A</i>	3740	3803	-2482
C(7) <i>A</i>	3744	3816	-3791
N(8) <i>A</i>	3779	3231	-4450
C(8a) <i>A</i>	3739	2624	-3837
C(11) <i>A</i>	3769	4469	-1729
C(12) <i>A</i>	3636	4491	-4521
C(1') <i>B</i>	1729	-1683	-986
C(2') <i>B</i>	377	-1302	-1995
O(2') <i>B</i>	-1402	-1647	-2334
C(3') <i>B</i>	1721	-1271	-3033
O(3') <i>B</i>	1567	-1921	-3686
C(4') <i>B</i>	3748	-1188	-2325
O(4') <i>B</i>	3602	-1401	-1050
C(5') <i>B</i>	4561	-449	-2261
O(5') <i>B</i>	3262	31	-1764
N(1) <i>B</i>	1324	-1607	317
C(2) <i>B</i>	1283	-946	833
O(2) <i>B</i>	932	-1336	4004
N(3) <i>B</i>	1155	-908	2092
C(4) <i>B</i>	1087	-1455	2918
O(4) <i>B</i>	1357	-405	237
C(4a) <i>B</i>	1219	-2145	2346
N(5) <i>B</i>	1253	-2716	3084
C(6) <i>B</i>	1495	-3333	2568
C(7) <i>B</i>	1750	-3383	1286
N(8) <i>B</i>	1654	-2820	556
C(8a) <i>B</i>	1390	-2201	1081
C(11) <i>B</i>	1534	-3973	3379
C(12) <i>B</i>	2193	-4067	698
H(1) <i>A</i>	4415	2528	-6051
H(2) <i>A</i>	5004	1033	-6085
H(3) <i>A</i>	4647	1113	-8274
H(4) <i>A</i>	1702	1987	-8417
H(5) <i>A</i>	-404	1122	-7705
H(6) <i>A</i>	901	811	-8739
H(7) <i>A</i>	7400	2100	-6320
H(8) <i>A</i>	4650	2220	-9020
H(9) <i>A</i>	1500	630	-6270
H(10) <i>A</i>	3208	910	-2324
H(11) <i>A</i>	3950	4440	-880
H(12) <i>A</i>	2550	4750	-1800
H(13) <i>A</i>	4980	4740	-1700
H(14) <i>A</i>	2720	4810	-4200
H(15) <i>A</i>	3110	4350	-5480
H(16) <i>A</i>	4800	4740	-4480
H(1) <i>B</i>	1737	-2198	-1200

Table 2 (cont.)

H(2) <i>B</i>	141	-809	-1703
H(3) <i>B</i>	1375	-872	-3609
H(4) <i>B</i>	4694	-1505	-2697
H(5) <i>B</i>	5839	-437	-1729
H(6) <i>B</i>	4747	-285	-3120
H(7) <i>B</i>	-1100	-2020	-2840
H(8) <i>B</i>	1500	-1870	-4400
H(9) <i>B</i>	2860	-150	-1050
H(10) <i>B</i>	1131	-425	2443
H(11) <i>B</i>	1250	-3900	4060
H(12) <i>B</i>	700	-4260	2980
H(13) <i>B</i>	2830	-4180	3500
H(14) <i>B</i>	1500	-4400	870
H(15) <i>B</i>	2270	-3960	-150
H(16) <i>B</i>	3480	-4200	1050

Table 3. *Bond distances* (Å)

Average standard deviations are 0.005 Å.

	Molecule <i>A</i>	Molecule <i>B</i>
Ribose		
C(1')-C(2')	1.538	1.535
C(2')-C(3')	1.536	1.537
C(3')-C(4')	1.527	1.524
C(4')-C(5')	1.513	1.518
C(5')-O(5')	1.432	1.429
C(4')-O(4')	1.461	1.451
O(4')-C(1')	1.418	1.411
C(2')-O(2')	1.400	1.406
C(3')-O(3')	1.415	1.424
Heterocycle		
C(1')-N(1)	1.466	1.474
N(1)-C(2)	1.378	1.381
C(2)-N(3)	1.381	1.376
N(3)-C(4)	1.372	1.379
C(4)-C(4a)	1.463	1.461
C(4a)-C(8a)	1.392	1.390
C(4a)-N(5)	1.350	1.350
N(5)-C(6)	1.314	1.321
C(6)-C(7)	1.414	1.420
C(7)-N(8)	1.327	1.329
N(8)-C(8a)	1.337	1.332
C(8a)-N(1)	1.407	1.400
C(2)-O(2)	1.217	1.213
C(4)-O(4)	1.221	1.222
C(6)-C(11)	1.510	1.503
C(7)-C(12)	1.509	1.500

6°; Arndt & Willis, 1966) and for geometrical factors, but not for absorption.

A sharpened Patterson map indicated that the lumazine ring systems of the two molecules in the asymmetric unit are arranged perpendicular to **a**, but their absolute position could not be determined. When *MULTAN* (Main, Germain & Woolfson, 1970) was tried with 446 E^2 's > 1.5 , only a chicken-wire-like distribution of peaks on planes perpendicular to **a** was obtained, but again the absolute position of the lumazine systems was obscured. The solution was finally achieved when all the Σ_1 contributions which

Table 4. Bond angles (°)

Average standard deviations are 0.3°.

	Molecule A	Molecule B
Ribose		
C(1')—C(2')—C(3')	99.9	99.6
C(2')—C(3')—C(4')	103.4	103.6
C(4')—C(5')—O(5')	113.3	111.6
C(4')—C(1')—C(2')	109.3	108.6
O(4')—C(1')—C(2')	106.4	105.6
C(1')—C(2')—O(2')	114.1	113.9
C(3')—C(2')—O(2')	115.3	114.3
C(2')—C(3')—O(3')	105.9	108.2
C(4')—C(3')—O(3')	111.6	110.5
C(3')—C(4')—C(5')	116.2	115.7
O(4')—C(4')—C(5')	108.4	106.4
C(4')—C(5')—O(5')	113.3	111.6
O(4')—C(1')—N(1)	108.4	106.6
C(2')—C(1')—N(1)	117.8	117.7
C(4')—O(4')—C(1')	109.3	108.6
Heterocycle		
N(1)—C(2)—N(3)	116.4	117.1
C(2)—N(3)—C(4)	128.6	127.6
N(3)—C(4)—C(4a)	113.1	113.7
C(4)—C(4a)—C(8a)	120.0	120.1
C(4a)—C(8a)—N(1)	121.3	121.1
C(4a)—C(4)—O(4)	125.7	126.6
C(8a)—C(4a)—N(5)	121.0	121.4
C(4a)—N(5)—C(6)	118.1	117.7
N(5)—C(6)—C(7)	120.6	120.5
C(6)—C(7)—N(8)	121.6	121.4
C(7)—N(8)—C(8a)	117.5	117.7
C(4a)—C(8a)—N(8)	121.1	121.2
C(2)—N(1)—C(1')	120.8	119.4
C(8a)—N(1)—C(1')	119.1	119.1
O(2)—C(2)—N(1)	123.7	123.8
N(3)—C(2)—O(2)	119.8	119.1
N(3)—C(4)—O(4)	121.2	119.8
C(4)—C(4a)—N(5)	118.9	118.4
N(5)—C(6)—C(11)	117.9	118.2
C(11)—C(6)—C(7)	121.5	121.2
C(6)—C(7)—C(12)	122.2	121.7
N(8)—C(7)—C(12)	116.2	116.8
N(1)—C(8a)—N(8)	117.6	117.7

Table 5. Some torsion angles (A—B—C—D)

These are defined as zero if bonds A—B and C—D are *cis*-planar and counted positive if, looking along the central bond B—C, the far bond is rotated clockwise with respect to the near bond.

Torsion angle	Molecule A	Molecule B
ν_2 C(1')—C(2')—C(3')—C(4')	-36.2°	-34.0°
ν_3 C(2')—C(3')—C(4')—O(4')	24.6	18.2
ν_4 C(3')—C(4')—O(4')—C(1')	-1.4	7.2
ν_0 C(4')—O(4')—C(1')—C(2')	-22.7	-30.1
ν_1 O(4')—C(1')—C(2')—C(3')	36.7	39.7
O(4')—C(4')—C(5')—O(5')	-67.8	-63.6
C(3')—C(4')—C(5')—O(5')	51.3	54.7
χ C(2)—N(1)—C(1')—O(4')	72.1	60.8
N(1)—C(1')—C(2')—O(2')	-77.9	-79.4
C(1')—C(2')—C(3')—O(3')	81.3	83.3
O(2')—C(2')—C(3')—O(3')	-41.5	-38.4
C(5')—C(4')—C(3')—O(3')	150.8	114.4
C(4')—C(3')—C(2')—O(2')	-159.0	-155.8

contained three very strong *h00* reflexions were removed from the data set and *MULTAN* was run again with only five starting reflexions.

In the 32 phase sets, the figure of merit varied from 0.746 to 0.967, the sum of the α 's ranged from 19.35 to 23.47 and the Karle *R* values ranged from 37.5 to 32.2%; ψ_0 values were not determined. Although the variation between the correct and false solutions is not very pronounced, the set with the best consistency criteria allowed the deduction of the whole structure.

The atomic parameters were refined by full-matrix least-squares techniques (Busing, Martin & Levy, 1972). All the H atoms were located from difference maps. The final *R* was 5.9% for all 4286 data.*

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32664 (27 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 6. Least-squares planes through the lumazine heterocycles and the best four ribose atoms

The planes are defined by atoms marked by a dagger and are based on a Cartesian system with *X* along **a**, *Y* along **b** and *Z* along **c**.*

The lumazine heterocycles

$$\text{Molecule A: } 0.9955X - 0.0543Y - 0.0772Z = 2.0920$$

$$\text{Molecule B: } 0.9968X + 0.0702Y + 0.0384Z = 0.7915$$

Deviations (Å) of atoms from planes

	Molecule A	Molecule B
C(1')	0.156	0.091
C(2')	1.090	-0.873
N(1)†	0.099	-0.068
C(2)†	-0.080	0.035
N(3)†	-0.048	0.057
C(4)†	0.004	0.006
C(4a)†	0.049	-0.044
C(8a)†	0.048	-0.039
N(5)†	0.029	-0.036
C(6)†	-0.017	0.006
C(7)†	-0.070	0.067
N(8)†	-0.013	0.016
O(2)	-0.242	0.006
O(4)	-0.023	0.109
C(11)	-0.035	0.015
C(12)	-0.245	0.231

The ribose atoms

$$\text{Molecule A: } 0.1088X + 0.9029Y - 0.4157Z = 6.3729$$

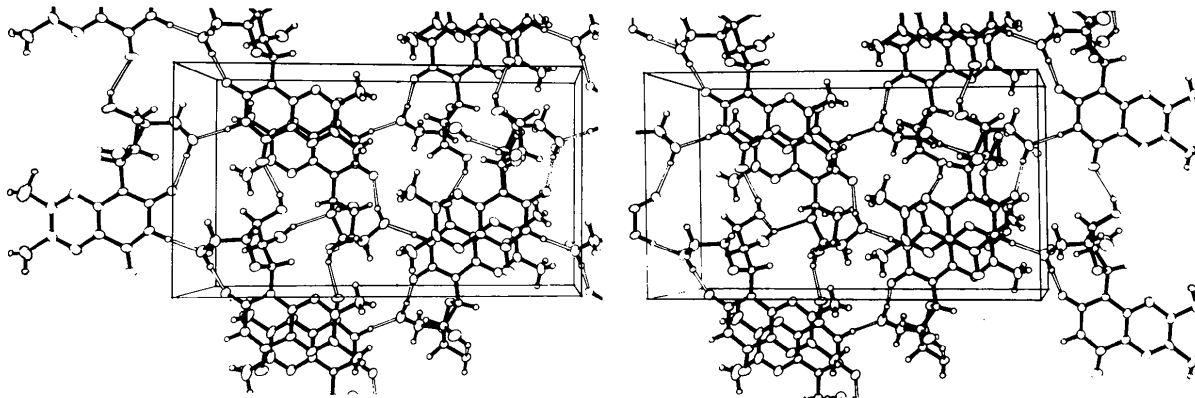
$$\text{Molecule B: } 0.3061X - 0.8915Y - 0.3338Z = 3.5214$$

Deviations (Å) of atoms from planes

	Molecule A	Molecule B
C(1')†	-0.0049	0.0245
C(2')	-0.5906	-0.5872
C(3')†	0.0045	-0.0227
C(4')†	-0.0074	0.0375
O(4')†	0.0078	-0.0395

Table 7. *Geometry of the hydrogen bonds*

Donor	Acceptor	$d(D\cdots A)$	$d(D-H)$	$d(H\cdots A)$	$\angle A\cdots H-D$	$\angle H-D\cdots A$	Symmetry operation of acceptor
O(2') <i>A</i>	O(3') <i>B</i>	2.847 Å	0.87 Å	2.00 Å	165°	11°	$1-x, -\frac{1}{2}+y, 1-z$
O(3') <i>A</i>	O(4) <i>A</i>	2.923	0.84	2.15	151	21	$x, y, 1+z$
O(5') <i>A</i>	O(2) <i>A</i>	2.800	0.90	2.06	138	29	Intramolecular
N(3) <i>A</i>	O(5') <i>B</i>	2.772	1.00	1.78	171	6	x, y, z
O(2') <i>B</i>	O(4') <i>A</i>	2.918	0.96	2.12	143	26	$1-x, \frac{1}{2}+y, 1-z$
O(2') <i>B</i>	O(3') <i>B</i>	2.703	0.96	2.16	101	46	$1+x, y, z$
O(3') <i>B</i>	O(4) <i>B</i>	2.724	0.77	2.00	156	18	$x, y, -1+z$
O(5') <i>B</i>	O(2) <i>B</i>	2.786	0.92	1.89	164	11	Intramolecular
N(3) <i>B</i>	O(5') <i>A</i>	2.779	1.00	1.80	166	9	x, y, z

Fig. 2. A stereo drawing of the unit-cell content viewed along a^* .

Scattering factors were from *International Tables for X-ray Crystallography* (1962) and the structure amplitudes were given weights according to counting statistics with 1% allowance for machine instability (Stout & Jensen, 1968).

Results

The atomic parameters are presented in Table 2; geometrical data are given in Tables 3 to 6. Table 7 contains the data for the hydrogen-bonding interactions which are also illustrated in the stereoview (Fig. 2).

Discussion

Details of the structure of (I) have been described and compared with those obtained for lumazine (Norrestam, Stensland & Söderberg, 1972) and uracil (Voet & Rich, 1970). Therefore, only additional features and intermolecular interactions will be considered here.

The two molecules in the asymmetric unit display similar parameters (Table 5), and are both in the *syn* conformation with C(2)–N(1)–C(1')–O(4') at 72.1

and 60.8°. Similar values for the same angle were observed in 6-methyluridine, 69.6 and 69.4° (Suck & Saenger, 1972), 3',5'-diacetyl-2'-deoxy-2'-fluorouridine, 68.5° (Suck *et al.*, 1974) and cytidine-2',3'-cyclophosphate, 62.9 and 74.5° (Coulter, 1973); in 4-thiouridine this angle is increased considerably to 92.9° (Saenger & Scheit, 1970). In Table 8 these torsion angles are listed together with the conformational angles within the ribose moieties. Clearly the C(3')-*endo* envelope, which dominates in *anti*-nucleosides, is not preferred in *syn*-nucleosides but is replaced by a C(3')-*endo*, C(4')-*exo* twist form and by the C(2')-*endo* envelope which both appear to avoid unfavourable contacts between O(2) and the H atom attached to C(3'). The ribose puckering for cytidine-2',3'-cyclophosphate (Coulter, 1973) differs from that of the other *syn*-nucleosides in Table 8, probably as a consequence of the fused phosphodiester group.

The lumazine heterocycles are not strictly planar: the normals to the pyrimidine and pyrazine rings form an angle of about 5°. From the data given in Table 6, it appears that the fold is along the line N(1)–C(8a)–C(4a)–N(5) rather than along C(8a)–C(4a).

The packing of the molecules follows the pattern frequently observed in nucleoside structures. The heterocycles are stacked 3.45 Å apart along a . These

Table 8. Comparison of the torsion angle χ and the ribose conformation in different syn-pyrimidine nucleosides

Molecule	For angle definitions see Table 6.						Sugar pucker	References
	χ	ν_0	ν_1	ν_2	ν_3	ν_4		
Title compound								
Molecule A	72.1°	-22.7°	36.7	-36.2°	24.6°	-1.4°	C(2')-endo	This work
Molecule B	60.8	-30.1	39.7	-34.0	18.2	7.2	C(2')-endo	
6-Methyluridine								
Molecule A	69.6	-25.8	36.9	-33.0	19.7	-3.6	C(2')-endo	Suck & Saenger (1972)
Molecule B	69.4	-18.6	34.3	-35.8	26.4	-5.2	C(2')-endo	
4-Thiouridine	92.4	-11.3	-14.9	33.1	-40.6	33.3	C(3')-endo, C(4')-exo	Saenger & Scheit (1970)
3',5'-Diacetyl-2'-deoxy-2'-fluorouridine	68.5	-12.1	-10.3	27.0	-34.5	29.7	C(3')-endo, C(4')-exo	
Cytidine-2',3'-cyclophosphate								
Molecule A	62.9	-33.2	16.1	5.5	-24.4	36.0	O(1')-endo	Coulter (1973)
Molecule B	74.5	1.9	-0.7	-0.7	1.8	-2.3	Planar	

columns of predominantly hydrophobic character are embedded into more hydrophilic zones built up by the ribose residues. These are linked by hydrogen bonds which also involve O(2), O(4) and the N(3)-H group of the lumazine heterocycles but not the pyrazine N(5) and N(8) atoms (Table 7).

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Structure Cristalline du Bis-thioacétate de Nickel β Picoline (1:2) Forme α

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$\text{Ni}(\text{CH}_3\text{COS})_2 \cdot 2\text{C}_6\text{H}_7\text{N}$ (α phase) is triclinic, space group $P\bar{1}$, with two molecules in a unit cell of dimensions $a = 8.596$ (2), $b = 14.337$ (2), $c = 8.279$ (3) Å, $\alpha = 92.54$ (2), $\beta = 114.04$ (2), $\gamma = 87.95$ (1)°. The structure was solved by the heavy-atom method from 4330 intensities collected with an automatic diffractometer. The final R is 0.032. The coordination of the Ni^{2+} ion is six. The O and N atoms are *cis*, while S atoms are *trans*.

Dans le cadre d'une étude thermo-chimique et structurale des thioacétates métalliques (Bernard, Borel & Ledésert, 1973; Borel & Ledésert, 1975), nous avons déterminé la structure du thioacétate de nickel solvato-

par la pyridine (Borel, Geffrouais & Ledésert, 1976), et la β et la γ picoline (formes b) (Borel, Geffrouais & Ledésert, 1977a,b).

L'intérêt des résultats réside surtout dans la dis-