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Note

Crystal and molecular structure of 1,4-dimethyl-3-(D-*galacto*-pentitol-1-yl)-5-(*p*-tolyl)pyrazole

Maria D. Estrada De Oya and Amparo Lopez-Castro
Departamento de Fisica de la Materia Condensada de la Universidad de Sevilla e Instituto de Ciencias de Materiales de Sevilla, C.S.I.C., Apartado 1065, 41080 Sevilla (Spain)

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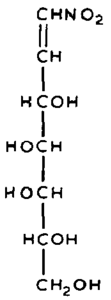
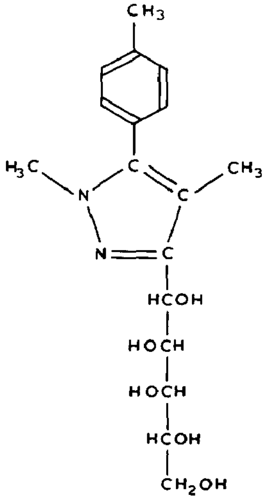
1,4-Dimethyl-3-(D-*galacto*-pentitol-1-yl)-5-(P-tolyl)pyrazole (**2**) was synthesised[1] by the reaction of formaldehyde tolylhydrazone, generated *in situ*, with 1,2-dideoxy-1-nitro-D-*galacto*-hept-1-enitol (**1**). 4-(Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1-phenylpyrazole has been studied by X-ray crystallography[2]. Compound **2** and related compounds are of interest as intermediates in the synthesis of *C*-nucleosides[3].



1



2

The structure **2** was assigned[1] on the basis of analytical, i.r., u.v., and ^{1}H- and ^{13}C-n.m.r. data, and in order to confirm the structure an X-ray analysis was carried out.

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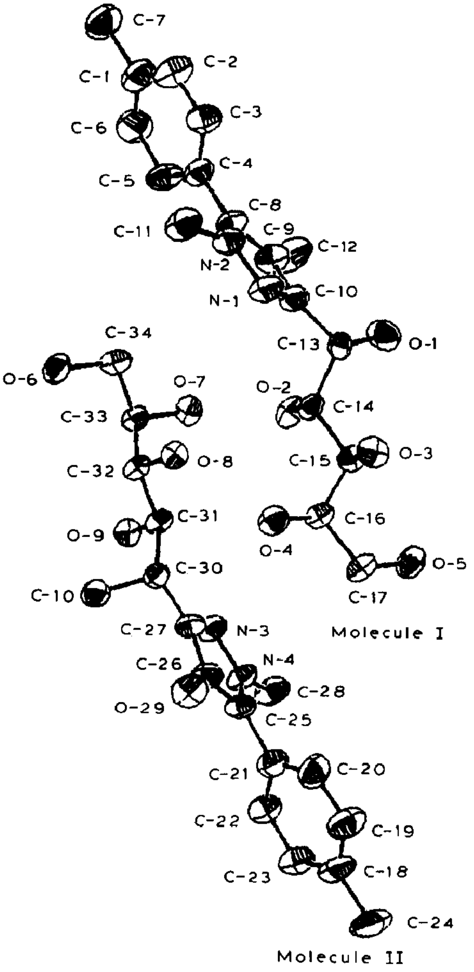
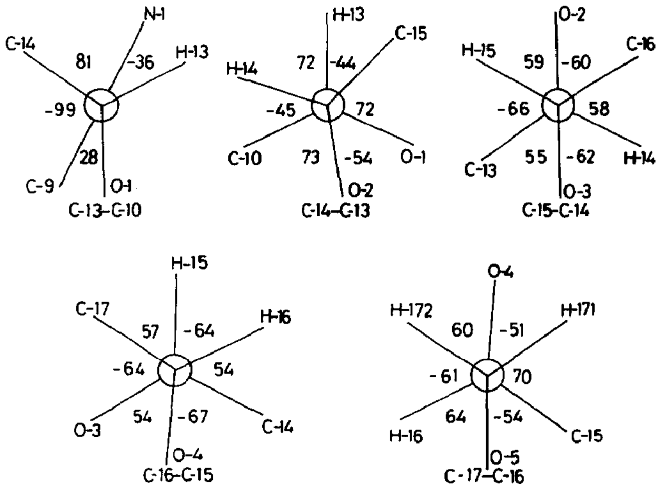


Fig. 1. ORTEP[13] view along the axis *b* of the two independent molecules in the asymmetric unit cell.

A perspective view of the two independent molecules that form the asymmetric unit, showing the relative conformation and the atomic numbering, is given in Fig. 1. The bond lengths and bond angles are listed in Tables I and II. The Newman projections corresponding to the C–C bonds of the sugar chains are shown in Fig. 2. According to the Klyne–Prelog[4] rules, the configurations of the chiral centres C-16, C-15, C-14, and C-13 in molecule I and C-33, C-32, C-31, and C-30 in molecule II are *R*, *S*, *R*, and *S*, respectively, in accordance with the D-*galacto* structure. The differences between molecules I and II involve the conformations of two hydroxyl groups (Figs. 1 and 2).

The pyrazole ring is planar in each molecule [maximum deviation from the respective least-squares plane, 0.014(10) and 0.014(11) Å]; C-4, C-11, C-12, and C-13 are at −0.102(11), 0.238(15), −0.008(17), and −0.069(9) Å, respectively, and C-21, C-28, C-29, and C-30 at −0.046(12), −0.030(14), 0.012(15), and −0.083(9) Å, respec-

(a) Molecule I



(b) Molecule II

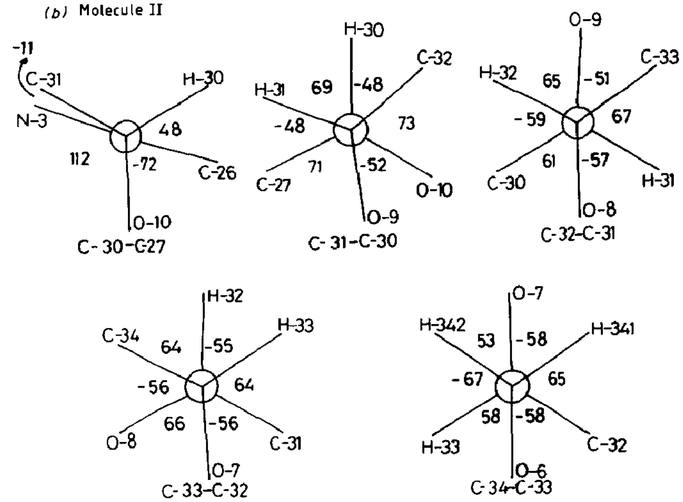


Fig. 2. Newman projections of the sugar chain in (*a*) molecule I and (*b*) molecule II.

tively. The average C–C and C–N bond lengths of 1.398(18) and 1.347(19) Å, respectively, and the N–N bond lengths of 1.356(13) Å are similar to those in other substituted pyrazoles and indicate a high degree of electron delocalisation.

The phenyl groups are planar [maximum deviation, 0.009(19) and 0.007(18) Å] and the C(methyl) atoms attached thereto are practically in the corresponding plane [maximum deviation, 0.052(20) and 0.011(23) Å]. The geometry of the tolyl group is normal, the C–C bond length is 1.388(23) Å, the C–C–C angle is 120.0(15)°, and the C–CH_3 bond length is 1.514(21) Å.

The sugar chains are also planar [maximum deviation from the corresponding

TABLE I

Bond lengths (Å) for **2**

O-1–C-13	1.416(18)	C-5–C-6	1.430(20)
O-2–C-14	1.417(17)	C-8–C-9	1.377(18)
O-3–C-15	1.438(17)	C-9–C-10	1.423(17)
O-4–C-16	1.426(17)	C-9–C-12	1.486(22)
O-5–C-17	1.426(18)	C-10–C-13	1.502(14)
O-6–C-34	1.436(16)	C-13–C-14	1.530(13)
O-7–C-33	1.424(15)	C-14–C-15	1.535(13)
O-8–C-32	1.437(13)	C-15–C-16	1.520(12)
O-9–C-31	1.418(14)	C-16–C-17	1.528(14)
O-10–C-30	1.454(13)	C-18–C-19	1.371(21)
N-1–N-2	1.362(13)	C-18–C-23	1.371(22)
N-1–C-10	1.333(15)	C-18–C-24	1.509(21)
N-2–C-8	1.375(19)	C-19–C-20	1.393(19)
N-2–C-11	1.462(21)	C-20–C-21	1.401(19)
N-3–N-4	1.351(13)	C-21–C-22	1.412(17)
N-3–C-27	1.339(19)	C-21–C-25	1.478(15)
N-4–C-25	1.342(17)	C-22–C-23	1.382(17)
N-4–C-28	1.463(20)	C-25–C-26	1.392(18)
C-1–C-2	1.374(23)	C-26–C-27	1.401(16)
C-1–C-6	1.361(22)	C-26–C-29	1.501(22)
C-1–C-7	1.519(20)	C-27–C-30	1.470(15)
C-2–C-3	1.394(19)	C-30–C-31	1.562(15)
C-3–C-4	1.381(17)	C-31–C-32	1.510(14)
C-4–C-5	1.385(21)	C-32–C-33	1.521(15)
C-4–C-8	1.487(15)	C-33–C-34	1.522(15)

least-squares plane, 0.045(14) and 0.033(10) Å]. The bond distances and angles in the sugar chain have the expected values and are not discussed.

The dihedral angles for the pyrazole–tolyl rings are 54.6(4)° and 55.5(4)°, and for the pyrazole–sugar groups are 94.6(8)° and 17.9(3)°.

The crystal cohesion is governed mainly by intermolecular hydrogen bonds (Table III). The molecules are stacked in layers that are parallel to the *ac* plane. The distance which separates the two layers is relatively large (0.5*b* = 4.72 Å). The cohesion forces of the packing between molecules in each layer are provided mostly by two double hydrogen bonds (between O-3 and O-6, and between O-2 and O-7) and two single hydrogen bonds (O-9···O-5 and O-4···O-8), which suggests that these interactions could be responsible for the conformation adopted by the two molecules in the asymmetric unit cell.

Since the structural analysis showed that the two independent molecules adopt different conformations in the crystal structure, a study of the energetics has been carried out in order to elucidate the origin of the difference. The theoretical atom–atom potential model proposed by Kitaigorodsky[5] was used, where a molecule can be considered as a quasi-rigid body. The interaction of molecules may be described as a sum of the pair-wise contributions between atom that belong to different molecules described by characteristic potential curves. Thus, the energy of the non-bonded

TABLE II

Bond angles (degrees) for **2**

N-1–N-2–C-11	120.4(9)	C-15–C-16–C-17	111.2(8)
N-1–N-2–C-8	110.4(9)	O-4–C-16–C-17	106.2(9)
C-8–N-2–C-11	127.7(10)	O-5–C-17–C-16	109.6(10)
N-4–N-3–C-27	106.1(9)	C-23–C-18–C-24	120.7(13)
N-3–N-4–C-28	120.0(10)	C-19–C-18–C-24	120.7(15)
N-3–N-4–C-25	111.7(10)	C-19–C-18–C-23	118.6(12)
C-25–N-4–C-28	128.3(9)	C-18–C-19–C-20	120.4(14)
C-6–C-1–C-7	121.3(14)	C-19–C-20–C-21	121.5(12)
C-2–C-1–C-7	120.8(13)	C-20–C-21–C-25	120.1(11)
C-2–C-1–C-6	117.8(13)	C-20–C-21–C-22	117.2(11)
C-1–C-2–C-3	122.3(14)	C-22–C-21–C-25	122.1(11)
C-2–C-3–C-4	118.9(13)	C-21–C-22–C-23	119.6(12)
C-3–C-4–C-8	119.5(11)	C-18–C-23–C-22	122.7(13)
C-3–C-4–C-5	121.1(11)	N-4–C-25–C-21	121.7(12)
C-5–C-4–C-8	119.4(11)	C-21–C-25–C-26	131.4(12)
C-4–C-5–C-6	117.3(13)	N-4–C-25–C-26	106.8(9)
C-1–C-6–C-5	122.5(15)	C-25–C-26–C-29	127.7(10)
N-2–C-8–C-4	120.4(12)	C-25–C-26–C-27	105.3(11)
C-4–C-8–C-9	132.4(12)	C-27–C-26–C-29	127.0(11)
N-2–C-8–C-9	107.0(10)	N-3–C-27–C-26	110.1(10)
C-8–C-9–C-12	127.3(11)	C-26–C-27–C-30	126.5(12)
C-8–C-9–C-10	105.9(12)	N-3–C-27–C-30	123.3(10)
C-10–C-9–C-12	126.8(12)	O-10–C-30–C-27	108.6(7)
N-1–C-10–C-9	109.6(10)	C-27–C-30–C-31	115.2(10)
C-9–C-10–C-13	134.6(13)	O-10–C-30–C-31	109.6(7)
N-1–C-10–C-13	115.9(11)	O-9–C-31–C-30	109.9(8)
O-1–C-13–C-10	111.8(9)	C-30–C-31–C-32	113.0(10)
C-10–C-13–C-14	111.4(7)	O-9–C-31–C-32	111.3(8)
O-1–C-13–C-14	112.9(10)	O-8–C-32–C-31	108.5(7)
O-2–C-14–C-13	109.9(9)	C-31–C-32–C-33	112.5(9)
C-13–C-14–C-15	113.8(7)	O-8–C-32–C-33	111.5(7)
O-2–C-14–C-15	111.1(9)	O-7–C-33–C-32	111.8(8)
O-3–C-15–C-14	109.3(9)	C-32–C-33–C-34	112.6(10)
C-14–C-15–C-16	111.9(7)	O-7–C-33–C-34	107.8(8)
O-3–C-15–C-16	108.0(9)	O-6–C-34–C-33	108.8(8)
O-4–C-16–C-15	111.1(9)		

TABLE III

Hydrogen bonding in the crystal of **2**

D···*A*		*D*···*A* (Å)	*H*···*A* (Å)	*D*–*H*···*A* (°)
O-9	O-5 (2)[a]	2.742(10)	1.858	152.9
O-4	O-8 (0)	2.883(10)	2.006	152.0
O-3	O-6 (1)	2.725(11)	1.833	154.4
O-6	O-3 (2)	2.725(11)	2.124	119.7
O-7	O-2 (0)	2.684(11)	1.851	144.2
O-2	O-7 (0)	2.684(11)	2.186	111.4

[a] Symmetry code: (0) x,y,z, (1) $x,y,z+1$, (2) $x,y,z-1$.

interactions is equal to the sum of the interactions of all pairs from both molecules:

$$U_{\text{non-bonded}} = \Sigma\, \Sigma f_m\,(r_{ij})$$

where f_m is the atom–atom potential, m indicates the type of interaction, and r_{ij} is the distance between atoms i and j. The potential function is in the form

$$f(r) = \mathrm{A}_{\alpha\beta}\, r^{-6} + \mathrm{B}_{\alpha\beta} \exp\,(-\mathrm{C}_{\alpha\beta}\, r)$$

where A–C are empirical parameters that depend on the atomic pair involved.

Rotation around C–C bonds in aliphatic molecules involves eclipsed conformations and energy barriers, so that an additional term for internal rotations was considered. In order to obtain values and forms of the barriers comparable with the experimental data, it was necessary to introduce into the potential function not only a term which depended on the distance between the nuclei (the sum of atom–atom interaction) but also a term that depended on the mutual positions of the vectors which connected the nuclei, *i.e.*, on the angles between groups of certain vectors. This additional term may be described as

$$U_{\text{tors}} = U^0{}_{\text{tors}} \cos{}^2\psi$$

where $U^0{}_{\text{tors}}$ is the energy for $\psi = 0$. So far, the potential function considers the interaction energy of pairs of non-bonded atoms and torsion energy as

$$U = U_{\text{non-bonded}} + U_{\text{tor}}$$

The results showed significant differences between the molecular energies calculated for the two conformations. The value for the molecule I was ~60% higher than that for molecule II. Although the calculated energy values can be considered as approximate only, they indicate that the conformation of molecule I has an energy significantly higher than that of molecule II, and that the different conformations in the crystal could be due to steric effects.

EXPERIMENTAL*

Crystals of $C_{17}H_{24}N_2O_5$ (M_r 336.4), m.p. 156–160°, $[\alpha]_D^{23}$ +4° (c 1, pyridine), were monoclinic with systematic absences consistent with $P2_1$. The crystal used was 0.08 × 0.16 × 0.14 mm. The lattice parameters, refined using 25 reflections within the range $2 < \theta < 12°$, were $a = 18.687(1)$, $b = 9.481(3)$, $c = 9.612(2)$ Å, and $\beta = 91.97(4)°$. The

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* The supplementary data including non-hydrogen atomic co-ordinates are deposited with, and can be obtained from, Elsevier Science Publishers, B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. References should be made to No. BBA/DD/473/ *Carbohydr. Res.*, 219 (1991) 215–222.

unit-cell volume V was 1702 Å^3, $Z = 4$, $D_c = 1.31$ g.cm^{-3}, and the absorption coefficient was 0.906 cm^{-1}.

An Enraf–Nonius CAD-4 diffractometer was used with monochromatic Mo-K_α radiation (0.7107 Å) and the $\omega - 2\theta$ scan technique at room temperature, ($0 \leqq h \leqq 22$, $0 \leqq k \leqq 10$, $-11 \leqq l \leqq 11$). Two standard reflections, monitored every 100 reflections, showed only statistical fluctuations. From 3273 unique reflections measured $(\sin \theta/\lambda)_{\max} = 0.60$ Å, 2667 were observed with $I \geqq 2\sigma(I)$. $F(000) = 720$. Corrections were made for Lorentz-polarisation effects, but nor for extinction and absorption.

The structure was solved by direct methods using the MULTAN-80 program[6]. Two independent molecules were located. The positional and anisotropic thermal parameters for all non-hydrogen atoms were refined by full-matrix least squares. The positions of the H atoms were calculated geometrically, except those of the hydroxyl groups which were calculated from a difference synthesis. All of the H atoms were assigned the same isotropic temperature factors as the atoms to which they were bonded, and were included in the refinement with positional and thermal parameters fixed (433 parameters). Refinement was based on F (structure amplitudes) to minimise the function $\Sigma\, w(|F_0| - |F_c|)^2$ with $w = 1/\sigma^2(F_0)$.

The refinement led to a final convergence with $R = 0.07$. All parameter shifts during the final cycle of refinement were <0.08; the residual electron density in the difference map was ± 0.3 e.Å^{-3}. Atomic scattering factors were taken from the International Tables for X-Ray Crystallography[7] and all calculations were carried out with the X-Ray System[8]. The y co-ordinate of N-1 was fixed in order to define the origin.

The energy evaluation was performed using the program PCK6[9], starting from the experimental structure.

The set of potential parameters include coefficients fitted by Williams[9] for C···C and H···H and by Govers[10] forN···N, and the parameters of Mason and Kreevoy[11] for O···O. For mixed interactions, the combination rules of Mirskaya[12] were used.

The energy was calculated including internal rotations of molecular fragments about selected bonds as axes. The selected bonds for molecule I were C-4–C-8 and C-13–C-14, and C-21–C-25 and C-30–C-31 for molecule II.

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