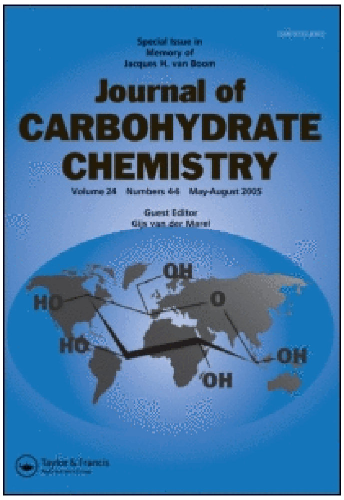

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X-Ray Crystallography of 3-(2-*0*-Acetyl-1, 3-Dibromo-1, 3-DI-Deoxy-L-*Erythro*-Glycerol-I-YL)-l-Phenyl-2-Pyrazoline-4, 5-Dione 4-(Phenylhydrazone)

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X-RAY CRYSTALLOGRAPHY OF 3-(2-*O*-ACETYL-1,3-DIBROMO-1,3-DIDEOXY-L-*ERYTHRO*-GLYCEROL-1-YL)-1-PHENYL-2-PYRAZOLINE-4,5-DIONE 4-(PHENYLHYDRAZONE)[1]

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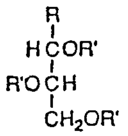
ABSTRACT

X-Ray crystallography confirmed the L-*erythro*-configuration of 3-(2-*O*-acetyl-1,3-dibromo-1,3-dideoxy-glycerol-1-yl)-1-phenyl-2-pyrazoline-4,5-dione 4-(phenylhydrazone) that results from the reaction of hydrogen bromide in acetic acid with the corresponding of L-*threo*-glycerol-1-yl analog.

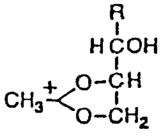
INTRODUCTION

The use of bromodeoxysugars in synthesis and the chemotherapeutic value of bromodeoxypolyols[2,3] and nucleosides[4-6] attracted our attention to the synthesis of bromodeoxy derivatives of acyclic C-nucleoside analogs,[7,8] such as those having triazole, flavazole and pyrazoline rings. In this paper we report on the confirmation of the absolute configuration of C-1 of the glycerolyl residue on the product from the reaction of hydrogen bromide in acetic acid with 3-(L-*threo*-glycerol-1-yl)-1-phenyl-2-pyrazoline-4,5-dione 4-(phenylhydrazone) (1).

RESULTS AND DISCUSSION



1 R' = H
2 R' = Ac



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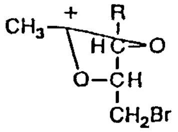

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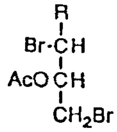

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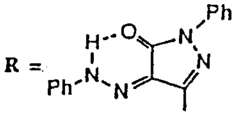

Treatment of 1 with hydrogen bromide in acetic acid gave a product (5) whose elemental analysis indicated its formulation as $C_{20}H_{18}Br_2N_4O_3$. The position of each bromine atom was deduced from a comparative study of the ^1H NMR spectrum of 5 with that of 1-phenyl-3-(1,2,3-tri-*O*-acetyl-L-*threo*-glycerol-1-yl)-2-pyrazoline-4,5-dione 4-(phenylhydrazone) (2). The spectrum of 5 showed the H-2 multiplet (δ 5.90) at a similar chemical shift to that of 2 (δ 5.85) indicating the location of the acetoxyl group on 5. The H-1 doublet of 5 (δ 5.42) is more shielded than H-2. This indicated that the two bromine atoms may be located on the C-1 and C-3 of the glycerolyl residue. The *erythro* configuration of 5 was confirmed by X-ray crystallography as shown in Experimental. The reaction of hydrogen bromide in acetic acid with a vicinal-diol may occur via partial acetylation to form a 1,3-dioxolan-2-ylium ion intermediate that gives a *trans* bromoacetate.[9,10]

Consequently, the mechanism of the reaction described here may proceed via the dioxolan-2-ylium ion 3, which after two successive reactions with bromide ion, gave 5 through 4.

EXPERIMENTAL

General Procedures. The melting point was determined with a Yanagimoto micro melting point apparatus and is uncorrected. ^{1}H NMR and IR spectra were recorded with JEOL GSX-270 and JASCO FT-IR8000S spectrometers, respectively.

3-(2-*O*-Acetyl-1,3-dibromo-1,3-dideoxy-L-*erythro*-glycerol-1-yl)-1-phenyl-2-pyrazoline-4,5-dione 4-(Phenylhydrazone) (5). A mixture of 1 (1.00 g) and hydrogen bromide in acetic acid (10 mL) was stirred for 2 h at room temperature and then left for overnight. The mixture was diluted with ice-cold water and the product was collected by filtration, washed with water and recrystallized from ethanol to give yellow-orange product (85% yield): mp 202-204 °C; ν_{max}(KBr) 1665 (OCN), 1740 cm^{-1} (OAc); ^{1}H NMR (CDCl$_3$) δ 2.04 (s, 3H, Ac), 4.08 (d, 2H, H-3,3'), 5.42 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1), 5.90 (m, 1 H, H-2), 7.29 and 7.96 (each m, 10H, Ar-H), 13.76 (s, 1H, NH).

Anal. Calcd for $C_{20}H_{18}Br_2N_4O_3$: C, 46.0; H, 3.5; N, 10.7. Found: C, 45.7; H, 3.2; N, 11.0.

X-Ray Analysis of 5. Single crystals were grown by slow evaporation of an ethanol solution at room temperature. Nicolet P3/F four circle diffractometer with graphite monochromated Cu Kα radiation. A prismatic crystal of approximately 0.35 x 0.25 x 0.15 mm in size was used. The space group was determined from systematic absences. Three standard reflections measured every 100 reflections decreased in intensities by 20%, thus a linear decay correction was applied. Of 2076

Table 1. Fractional Atomic Coordinates and equivalent isotropic thermal parameters ($Å^2$) with e.s.d's in parentheses.

$$Beq = 8/3\pi^2\Sigma_i\Sigma_jU_{ij}a^*_ia^*_ia_ia_j$$

	x	y	z	B_{eq}
N1	-0.405(2)	0.7473(8)	0.1029(3)	3.8(5)
N2	-0.390(3)	0.6151(10)	0.1078(3)	4.8(5)
C3	-0.210(3)	0.5961(11)	0.1289(3)	4.0(6)
C4	-0.089(4)	0.7141(10)	0.1411(3)	4.1(6)
C5	-0.225(3)	0.8105(11)	0.1221(4)	3.9(5)
C6	-0.591(3)	0.7961(13)	0.0799(4)	4.1(6)
C7	-0.761(4)	0.7150(15)	0.0616(5)	4.8(6)
C8	-0.943(4)	0.7625(16)	0.0400(4)	5.9(7)
C9	-0.954(4)	0.8933(17)	0.0329(4)	6.3(8)
C10	-0.797(5)	0.9736(17)	0.0505(6)	7.9(9)
C11	-0.616(4)	0.9275(13)	0.0747(4)	6.3(7)
C12	-0.140(3)	0.4644(9)	0.1412(3)	3.7(5)
C13	-0.203(3)	0.3653(12)	0.1131(5)	5.2(6)
C14	-0.171(4)	0.2286(11)	0.1279(5)	5.9(7)
Br15	-0.3330(5)	0.42856(15)	0.18563(4)	6.14(8)
O16	-0.044(2)	0.3901(8)	0.0844(2)	4.3(4)
C17	-0.151(5)	0.3493(15)	0.0521(4)	6.7(8)
O18	-0.345(4)	0.2917(16)	0.0489(5)	11.5(9)
C19	0.066(5)	0.3858(19)	0.0260(5)	8.9(9)
Br20	0.1652(5)	0.19742(16)	0.14301(8)	9.26(12)
N21	0.100(2)	0.7174(9)	0.1649(3)	3.9(5)
N22	0.185(3)	0.8309(9)	0.1715(3)	5.0(5)
C23	0.380(3)	0.8486(15)	0.1954(4)	4.8(6)
C24	0.496(4)	0.9633(15)	0.2005(4)	6.8(7)
C25	0.694(4)	0.9872(19)	0.2233(5)	7.6(8)
C26	0.779(3)	0.8764(26)	0.2438(5)	9.2(9)
C27	0.659(5)	0.7650(18)	0.2419(6)	9.1(9)
C28	0.481(4)	0.7506(15)	0.2158(4)	5.9(7)
O29	-0.189(3)	0.9262(8)	0.1248(2)	5.8(5)

Table 2. Bond Distances (Å) and Bond Angles (°) with e.s.d's in parentheses.

	distance		distance
N1----N2	1.41(2)	C12----Br15	2.00(2)
N1----C5	1.37(2)	C13----C14	1.56(3)
N1----C6	1.41(2)	C13----O16	1.40(2)
N2----C3	1.25(2)	C14----Br20	1.89(2)
C3----C4	1.47(2)	O16----C17	1.41(3)
C3----C12	1.51(2)	C17----O18	1.19(4)
C4----C5	1.43(2)	C17----C19	1.56(3)
C4----N21	1.34(2)	N21----N22	1.30(2)
C5----O29	1.24(2)	N22----C23	1.38(2)
C6----C7	1.42(3)	C23----C24	1.37(3)
C6----C11	1.41(3)	C23----C28	1.40(3)
C7----C8	1.35(3)	C24----C25	1.37(3)
C8----C9	1.41(3)	C25----C26	1.47(3)
C9----C10	1.36(3)	C26----C27	1.34(3)
C10----C11	1.41(3)	C27----C28	1.37(3)
C12----C13	1.53(2)		

	angle		angle
N2--N1--C5	112.2(12)	C3--C12--C13	111.4(13)
N2--N1--C6	118.8(12)	C3--C12--Br15	108.0(10)
C5--N1--C6	129.1(13)	C13--C12--Br15	109.9(10)
N1--N2--C3	106.4(13)	C12--C13--C14	111.3(14)
N2--C3--C4	112.8(14)	C12--C13--O16	106.1(13)
N2--C3--C12	121.7(15)	C14--C13--O16	112.8(14)
C4--C3--C12	125.4(14)	C13--C14--Br20	111.8(13)
C3--C4--C5	103.4(13)	C13--O16--C17	111.7(14)
C3--C4--N21	123.4(14)	O16--C17--O18	125.8(25)
C5--C4--N21	133.2(14)	O16--C17--C19	100.0(17)
N1--C5--C4	105.1(13)	O18--C17--C19	133.8(25)
N1--C5--O29	129.1(14)	C4--N21--N22	113.9(13)
C4--C5--O29	125.7(14)	N21--N22--C23	120.3(17)
N1--C6--C7	121.2(15)	N22--C23--C24	123.0(17)
N1--C6--C11	120.7(15)	N22--C23--C28	122.9(16)
C7--C6--C11	118.1(16)	C24--C23--C28	114.1(17)
C6--C7--C8	121.0(18)	C23--C24-C25	126.1(19)
C7--C8--C9	120.6(19)	C24--C25--C26	114.4(19)
C8--C9--C10	119.5(20)	C25--C26--C27	121.6(22)
C9--C10--C11	120.9(20)	C26--C27--C28	117.6(22)
C6--C11--C10	119.6(18)	C23--C28--C27	125.1(19)

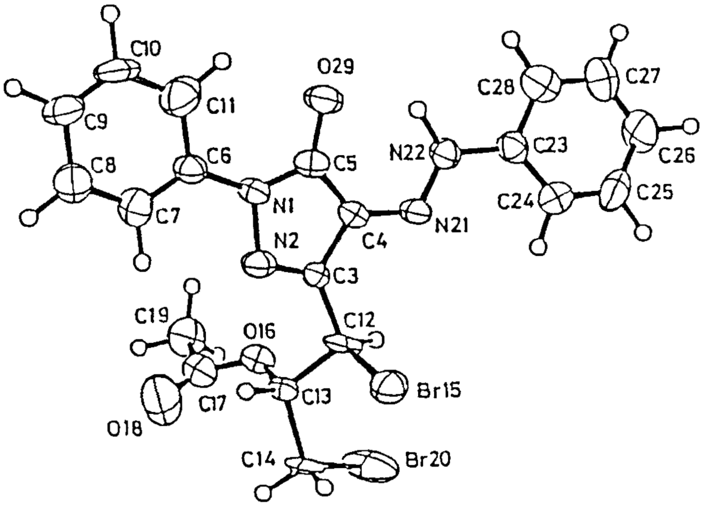

Fig. 1. ORTEP drawing of 5

independent reflections measured within $1^{\circ} < 2\theta < 150^{\circ}$, 1501 had intensities greater than $3\sigma(|Fo|)$ and were used for the structure analysis. The structure was solved by the direct method and refined by full-matrix least-squares method.[11] Hydrogen atoms were located at the geometrically expected positions. They were included in the Fc calculation, though excluded from the refinement. The weighting scheme used in the final stage was $w=1/\sigma^2(Fo) + 0.0027(Fo)^2$. The absolute configuration was determined from comparison of precisely measured intensities for sixteen unique Friedel pairs, all of which indicated the L-*erythro* configuration.

Crystal data: $C_{20}H_{18}Br_2N_4O_3$, M_r=522.2, Orthorhombic $P2_12_12_1$, a=5.261(1), b=10.565(2), c=37.693(8) Å, U=2095.1(6) Å^3, Z=4, Dx=1.66 Mgm^{-3}, λ(Cu Kα)=1.5418 Å, μ(Cu Kα)=48.3 cm^{-1}, F(000)=1040, T=298K, R=0.088, wR=0.094.

The final atomic parameters are listed in Table 1. Three bond lengths and angles are listed in Table 2. The ORTEP drawing[12] of the molecule with the numbering is shown in Fig. 1.

The substituted glycerolyl moiety is in an *erythro* configuration, which confirmed the prediction based on the proposed intermediate 3. The 1-(phenyl)-2-pyrazoline-4,5-dione 4-(phenylhydrazone) moiety (N1-C12, N21-O29) is nearly planar with the maximum deviation of 0.27 Å. The substituted glycerolyl moiety is out of this plane with the torsion angles in C4-C3-C12-C13 and C3-C12-C13-C14 of -153.8° and -171.1°, respectively. An intramolecular hydrogen bond is formed between N22 and O29(2.83Å).

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