Crystal structure of diethyl 2-(4,5-dihydroxy-2-methylsulfanyl-3,4,5,6-tetrahydro-4*H*-thiopyranyl)difluoromethylphosphonate, $C_{11}H_{21}F_2O_5PS_2$, *a thioglycoside analogue bearing a difluorophosphonate group*

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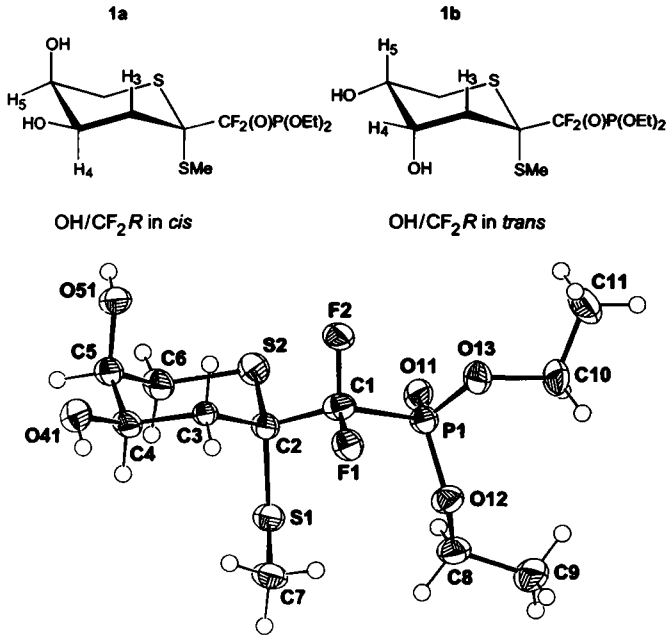

Abstract

$C_{11}H_{21}F_2O_5PS_2$, monoclinic, $P12_1/c1$ (no. 14), $a = 7.607(2)$ Å, $b = 7.711(2)$ Å, $c = 26.981(5)$ Å, $\beta = 97.19(3)°$, $V = 1570.2$ Å^3, $Z = 4$, $R_{gt}(F) = 0.058$, $wR_{ref}(F^2) = 0.161$, $T = 113$ K.

Source of material

The title compound has been obtained by hetero Diels-Alder reaction between the diethyl phosphonodifluorodithioacetate and the butadiene followed by *cis*-dihydroxylation using the modified Sharpless conditions [1]. Single crystals were obtained at room temperature by slow evaporation of a concentrated methanol/hexane solution.

Discussion

Due to the importance of carbohydrates in biological systems and their involvement in several diseases, disruption of their biosynthetic pathway by elaboration of glycosyltransferase inhibitors has shown a growing interest in the drug design discovery [2]. In that field, we have been interested in the synthesis of sulfur-containing difluoromethylphosphonate glycosides such as the title compound. The *cis*-dihydroxylation reaction using the modified Sharpless conditions gave a mixture of two compounds in 8:2 ratio separable by chromatography. These diastereoisomers **1a** and **1b** resulted from the position α or β of the two hydroxyls (figure, top). By assuming that the less bulky SCH_3 substituent on the anomeric carbon was placed in an axial position, the structure of the major diastereoisomer **1a** has been studied by X-ray diffraction to assign the relationship between the hydroxyls and the difluorophosphonate group. The results allowed us to confirm the *cis* relative configuration of the two hydroxyl groups with the difluoromethylphosphonate group, and to assign a (*R,R,S*) absolute configuration for the three stereogenic centers (C2, C4 and C5) created during the reaction sequence (figure, bottom).

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Table 1. Data collection and handling.

Crystal:	colorless, parallelepipedic, size 0.060 × 0.180 × 0.200 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	4.79 cm^{-1}
Diffractometer, scan mode:	Enraf-Nonius CAD4, $\omega/2\theta$
$2\theta_{max}$:	47.68°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	4150, 2338
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 1722
$N(param)_{refined}$:	190
Programs:	SHELXS-97 [3], SHELXL-97 [4], ORTEP-III [5]

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
H(41)	4*e*	−0.2961	1.2604	0.1778	0.056
H(51)	4*e*	−0.5741	0.8390	0.2450	0.053
H(3A)	4*e*	−0.2202	1.0186	0.1294	0.037
H(3B)	4*e*	−0.3975	0.9215	0.1402	0.037
H(4)	4*e*	−0.1351	1.0551	0.2177	0.036
H(5)	4*e*	−0.3438	1.0059	0.2740	0.037
H(6A)	4*e*	−0.2980	0.7056	0.2830	0.043
H(6B)	4*e*	−0.1216	0.7941	0.2683	0.043
H(7A)	4*e*	0.2691	0.9746	0.1474	0.060
H(7B)	4*e*	0.0724	1.0509	0.1367	0.060
H(7C)	4*e*	0.1352	0.9018	0.1016	0.060
H(8A)	4*e*	0.2319	0.3874	0.1426	0.046
H(8B)	4*e*	0.3338	0.5506	0.1227	0.046
H(9A)	4*e*	0.4685	0.2947	0.1005	0.068
H(9B)	4*e*	0.3804	0.3904	0.0509	0.068
H(9C)	4*e*	0.2838	0.2271	0.0722	0.068
H(10A)	4*e*	−0.0774	0.2804	−0.0058	0.050
H(10B)	4*e*	−0.0797	0.1750	0.0455	0.050
H(11A)	4*e*	−0.2833	0.0588	−0.0193	0.087
H(11B)	4*e*	−0.3873	0.2396	−0.0230	0.087
H(11C)	4*e*	−0.3811	0.1241	0.0265	0.087

Table 3. Atomic coordinates and displacement parameters (in $Å^2$).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
S(1)	4*e*	0.0684(2)	0.7828(2)	0.17643(5)	0.0260(6)	0.0246(7)	0.0496(8)	0.0017(5)	0.0029(5)	−0.0007(6)
S(2)	4*e*	−0.2491(2)	0.6196(2)	0.20333(5)	0.0422(7)	0.0210(7)	0.0501(8)	−0.0006(6)	0.0110(6)	0.0013(6)
P(1)	4*e*	−0.0935(2)	0.4631(2)	0.09675(5)	0.0290(7)	0.0186(7)	0.0467(8)	−0.0001(5)	0.0083(5)	−0.0019(6)
F(1)	4*e*	−0.1597(3)	0.7861(3)	0.0695(1)	0.039(2)	0.022(2)	0.044(2)	−0.000(1)	0.007(1)	0.002(1)
F(2)	4*e*	−0.3828(3)	0.6468(4)	0.0941(1)	0.025(1)	0.029(2)	0.055(2)	0.002(1)	0.001(1)	−0.007(1)
O(11)	4*e*	−0.0986(4)	0.3410(4)	0.1383(1)	0.037(2)	0.021(2)	0.048(2)	0.002(2)	0.013(2)	−0.001(2)
O(12)	4*e*	0.0948(4)	0.5049(4)	0.0826(1)	0.028(2)	0.027(2)	0.051(2)	0.001(2)	0.011(2)	0.002(2)
O(13)	4*e*	−0.2015(4)	0.4115(4)	0.0459(1)	0.036(2)	0.025(2)	0.053(2)	0.006(2)	0.005(2)	−0.009(2)
O(41)	4*e*	−0.3498(4)	1.1992(4)	0.1968(1)	0.040(2)	0.017(2)	0.058(2)	0.005(2)	0.013(2)	0.003(2)
O(51)	4*e*	−0.5287(4)	0.9026(4)	0.2248(1)	0.027(2)	0.025(2)	0.054(2)	0.001(1)	0.009(2)	0.001(2)
C(1)	4*e*	−0.2044(6)	0.6746(6)	0.1062(2)	0.028(3)	0.021(3)	0.049(3)	0.000(2)	0.008(2)	0.006(2)
C(2)	4*e*	−0.1709(6)	0.7659(6)	0.1569(2)	0.024(2)	0.020(3)	0.044(3)	0.002(2)	0.003(2)	−0.003(2)
C(3)	4*e*	−0.2718(6)	0.9421(6)	0.1533(2)	0.023(2)	0.016(3)	0.054(3)	−0.001(2)	0.011(2)	−0.009(2)
C(4)	4*e*	−0.2623(6)	1.0347(6)	0.2046(2)	0.028(2)	0.019(3)	0.043(3)	−0.002(2)	0.004(2)	−0.001(2)
C(5)	4*e*	−0.3485(6)	0.9341(6)	0.2430(2)	0.029(3)	0.019(3)	0.045(3)	0.001(2)	0.006(2)	−0.001(2)
C(6)	4*e*	−0.2461(7)	0.7654(6)	0.2558(2)	0.034(3)	0.020(3)	0.052(3)	0.002(2)	0.003(2)	−0.001(2)
C(7)	4*e*	0.1451(6)	0.9463(7)	0.1359(2)	0.027(3)	0.030(3)	0.062(4)	−0.006(2)	0.003(2)	−0.002(3)
C(8)	4*e*	0.2593(6)	0.4486(7)	0.1122(2)	0.025(3)	0.034(3)	0.057(3)	0.000(2)	0.006(2)	−0.003(3)
C(9)	4*e*	0.3564(7)	0.3300(7)	0.0813(2)	0.035(3)	0.036(3)	0.067(4)	0.007(2)	0.011(3)	−0.003(3)
C(10)	4*e*	−0.1503(7)	0.2511(7)	0.0210(2)	0.048(3)	0.026(3)	0.051(3)	0.004(2)	0.014(2)	−0.010(2)
C(11)	4*e*	−0.3144(8)	0.1607(8)	−0.0005(2)	0.051(4)	0.036(3)	0.083(5)	−0.003(3)	−0.004(3)	−0.025(3)

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