Crystal structure of (–)-4*R*,5*R*-(2*R*,3*R*-butylenedioxy)-3,7-dimethyl-tetrahydropurine-2,6,8-trione, $C_{11}H_{16}N_4O_5$

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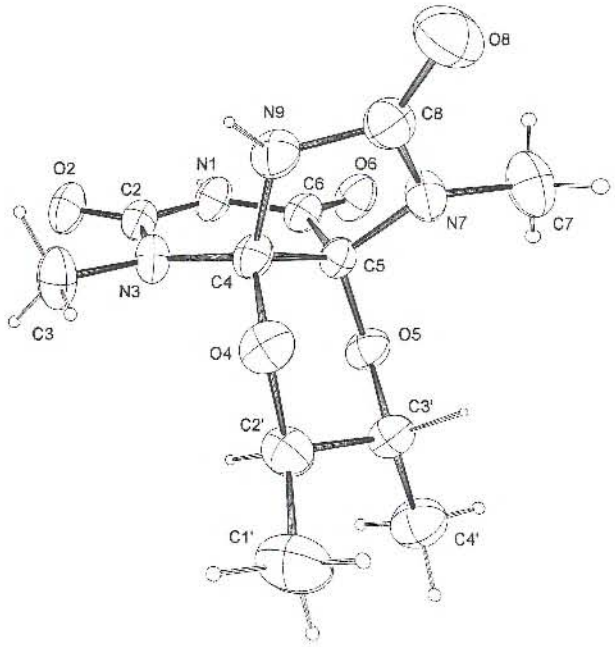
Received April 8, 1999, CCDC-No. 1267/161



Abstract

$C_{11}H_{16}N_4O_5$, orthorhombic, $P2_12_12_1$ (No. 19), a = 6.625(1) Å, b = 14.297(4) Å, c = 14.377(3) Å, V = 1361.8 Å^3, Z = 4, ρ_m = 1.390 g·m^{-3}, $R_{gt}(F)$ = 0.040, $wR(F^2)$ = 0.081, T = 293 K.

Source of material

Synthesis was done according to [1, 2]. Actually, only one diastereomeric propellane, $C_{11}H_{16}N_4O_5$, mp 529 K – 530 K, $[\alpha]_D$ –61° (c = 1, EtOH), was obtained through reaction of 5-chloro-3,7-dimethyl-5,7-dihydro-3*H*-purine-2,6,8-trione with anhydrous (–)-2*R*,3*R*-butanediol as the chiral auxiliary. The remarkable stereospecificity in cyclisation with a sec-glycol shows that the barrier for the conformational change depends on both *N*- and *O*-substitution. Recrystallisation from water gave crystals suitable for X-ray analysis. Chiral composite ureide chromophore of the compound was characterised by its circular dichroism (CD) spectrum in water: 202.8 (Δε +7.6), 218.4 (Δε +9.3), 254.8(Δε –5.5) nm.

Discussion

Studies of molecular conformation in crystals have shown that the covalent diadducts of dehydrourate exist in two isomeric ring-twisted forms of the flexible *cis*-fused system, having inverse signs of torsion angles of junction [4-9]. This implies that a conformational change acts as a switch controlling the mode of ring opening, thus accounting for the ramification of biological uricolytic pathways [1-3]. Current ideas about the steric course of uricolysis are based on three-dimensional structure of the uricase-inhibitor complex [10], which shows that an apparently normal hydration attack to the *re-re* face of dehydrourate has been frozen at about the transition state. The (5*R*)-adduct [11] as first formed can only reasonably undergo a further hydration to the elusive *cis*-4*R*,5*R*-dihydroxytetrahydropurine-2,6,8-trione derivative.

The structure of the title compound, a conformationally rigid propellane type diadduct with 2*R*,3*R*-butanediol, represents an (*R*,*R*)-configurational archetype of the transient uricolytic intermediate. Its particular ring-twisted conformation "a" [4, 8] is defined by nearly orthogonal torsion angle C6–C5–C4–N9 = –90.5(3)° and by torsion angles of junction N3–C4–C5–C6 30.4(3)°, N7–C5–C4–N9 27.8(5)°, and O4–C4–C5–O5 36.5(3)°. The pyrimidine adopts a conformation nearest 4-sofa and the imidazolinone moiety adopts a flattened half-chair conformation. The 1,4-dioxane ring, serving as an internal 2′*R*,3′*R*-configurational standard, has a distorted chair conformation with N3 and N7 disposed axially, and the C6, N9, C1′, and C4′ substituents in equatorial positions. Selected interatomic distances and torsion angles are as follows: N3–C4 1.454(4) Å, C4–N9 1.428(4) Å, C4–O4 1.403(4) Å, C4–C5 1.558(4) Å, C5–C6 1.536(4) Å, C5–O5 1.391(4) Å, C5–N7 1.457(4) Å; N3–C4–N9 112.7(3)°, C5–N7–C7 124.4(3)°, O4–C4–C5–C6 153.9(2)°, C2–N3–C4–N9 81.9(4)°, N3–C4–C5–O5 –86.9(3)°, N9–C4–O4–C2′ –158.3(3)°. Hydrogen bonding pattern: H1···O2 = 2.030(4) Å, N1···O2 = 2.866(4) Å, N3–H3···O2 = 163.0(3)° (1/2+*x*, 1/2–*y*, 1–*z*); H9···O6 = 2.085(4) Å, N9···O6 = 2.922(4) Å, N9–H9···O6 = 158.1(3)° (*x*–1, *y*, *z*).

Table 1. Data collection and handling.

Crystal:	colourless prism, size 0.35 × 0.40 × 0.50 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	1.11 cm^{-1}
Diffractometer, scan mode:	Philips PW1100 updated by Stoe, θ/2θ
$2\theta_{max}$:	60.06°
$N(hkl)_{measured}$, $N(hkl)_{unique}$	2265, 2265
Criterion for I_{obs}, $N(hkl)_{gt}$	$I_{obs} > 2\,\sigma(I_{obs})$, 1200
$N(param)_{refined}$:	181
Programs:	SIR88 [12], SHELXL-96 [13]

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

Atom	Site	x	y	z	U_{iso}
H(1)	4*a*	0.6346(4)	0.3277(2)	0.4728(2)	0.0380(7)
H(9)	4*a*	0.0794(4)	0.5364(2)	0.4813(1)	0.0353(6)
H(3A)	4*a*	0.0473(5)	0.4502(2)	0.6647(3)	0.0488(9)
H(3B)	4*a*	0.1334(5)	0.3502(2)	0.6854(3)	0.0488(9)
H(3C)	4*a*	0.0134(5)	0.3688(2)	0.5932(3)	0.0488(9)
H(7A)	4*a*	0.7837(7)	0.6682(3)	0.4568(3)	0.056(1)
H(7B)	4*a*	0.6167(7)	0.7387(3)	0.4243(3)	0.056(1)
H(7C)	4*a*	0.6774(7)	0.6545(3)	0.3603(3)	0.056(1)

Table 2. Continued.

Atom	Site	x	y	z	U_{iso}
H(2′)	4*a*	0.4490(5)	0.5199(3)	0.7411(2)	0.0374(8)
H(3′)	4*a*	0.5639(5)	0.6884(2)	0.6389(2)	0.0344(7)
H(1′A)	4*a*	0.1998(6)	0.6059(3)	0.8160(2)	0.0540(9)
H(1′B)	4*a*	0.2778(6)	0.6976(3)	0.7682(2)	0.0540(9)
H(1′C)	4*a*	0.4120(6)	0.6467(3)	0.8424(2)	0.0540(9)
H(4′A)	4*a*	0.8852(6)	0.6668(3)	0.7125(3)	0.0473(9)
H(4′B)	4*a*	0.8134(6)	0.5767(3)	0.7652(3)	0.0473(9)
H(4′C)	4*a*	0.7307(6)	0.6751(3)	0.7947(3)	0.0473(9)

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}
O(2)	4*a*	0.3532(4)	0.2681(2)	0.5541(2)	0.048(1)	0.028(1)	0.071(2)	–0.008(1)	–0.004(1)	0.004(1)
O(4)	4*a*	0.2667(3)	0.5750(2)	0.6404(2)	0.023(1)	0.041(1)	0.043(1)	0.004(1)	–0.001(1)	–0.006(1)
O(5)	4*a*	0.6792(3)	0.5645(2)	0.6038(2)	0.025(1)	0.040(1)	0.038(1)	–0.006(1)	–0.004(1)	–0.005(1)
O(6)	4*a*	0.8089(4)	0.4724(2)	0.4432(2)	0.032(1)	0.048(1)	0.057(2)	–0.009(1)	0.010(1)	–0.011(1)
O(8)	4*a*	0.2401(4)	0.6581(2)	0.3702(2)	0.063(2)	0.059(2)	0.055(2)	0.006(2)	–0.011(2)	0.018(1)
N(1)	4*a*	0.5685(4)	0.3743(2)	0.4956(2)	0.036(1)	0.025(1)	0.053(2)	0.001(1)	0.001(2)	–0.006(1)
N(3)	4*a*	0.2975(4)	0.4208(2)	0.5895(2)	0.030(1)	0.030(1)	0.044(1)	0.006(1)	0.003(1)	0.005(1)
N(7)	4*a*	0.5045(4)	0.6171(2)	0.4672(2)	0.035(1)	0.031(1)	0.045(2)	0.004(1)	0.001(1)	0.010(1)
N(9)	4*a*	0.2108(4)	0.5453(2)	0.4850(2)	0.026(1)	0.038(1)	0.045(2)	0.001(1)	0.009(1)	0.004(1)
C(2)	4*a*	0.3989(5)	0.3507(2)	0.5476(2)	0.030(2)	0.028(1)	0.042(2)	0.000(1)	0.006(2)	0.002(1)
C(3)	4*a*	0.1064(5)	0.3958(2)	0.6372(3)	0.035(2)	0.044(2)	0.062(2)	0.008(2)	0.016(2)	0.004(2)
C(4)	4*a*	0.3247(5)	0.5187(2)	0.5651(2)	0.021(1)	0.030(2)	0.038(2)	0.002(1)	0.004(2)	0.000(1)
C(5)	4*a*	0.5439(4)	0.5420(2)	0.5333(2)	0.026(1)	0.028(1)	0.033(2)	0.005(1)	0.000(1)	0.001(1)
C(6)	4*a*	0.6532(4)	0.4605(2)	0.4853(2)	0.023(1)	0.032(1)	0.039(2)	0.001(1)	0.003(1)	0.002(1)
C(7)	4*a*	0.6608(7)	0.6744(3)	0.4239(3)	0.052(2)	0.049(2)	0.067(2)	0.009(2)	0.012(2)	0.019(2)
C(8)	4*a*	0.3106(6)	0.6127(2)	0.4337(2)	0.040(2)	0.031(2)	0.043(2)	0.005(2)	0.005(2)	0.002(2)
C(2′)	4*a*	0.4138(5)	0.5817(3)	0.7158(2)	0.031(2)	0.046(2)	0.036(2)	0.000(2)	0.003(2)	0.002(2)
C(3′)	4*a*	0.6018(5)	0.6261(2)	0.6760(2)	0.033(2)	0.032(2)	0.035(2)	0.003(1)	0.002(1)	0.007(1)
C(1′)	4*a*	0.3177(6)	0.6381(3)	0.7925(2)	0.044(2)	0.077(3)	0.041(2)	0.005(2)	0.001(2)	0.009(2)
C(4′)	4*a*	0.7732(6)	0.6375(3)	0.7428(3)	0.039(2)	0.054(2)	0.050(2)	0.007(2)	0.007(2)	0.010(2)

Acknowledgment. The financial support of the Croatian Ministry of Science and Technology is gratefully acknowledged.

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