Crystal structure of theophylline-7-acetic acid, $C_9H_{10}N_4O_4$

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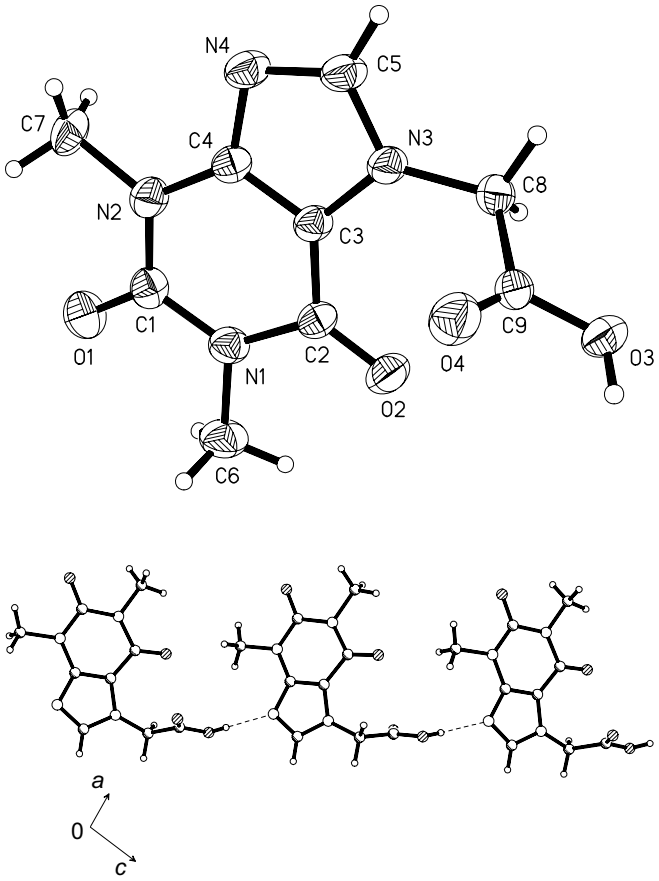

Abstract

$C_9H_{10}N_4O_4$, monoclinic, $P12_1/n1$ (no. 14),
a = 9.542(1) Å, b = 7.2415(9) Å, c = 14.446(2) Å,
β = 98.657(2)°, V = 986.8 Å^3, Z = 4, $R_{gt}(F)$ = 0.053,
$wR_{ref}(F^2)$ = 0.138, T = 298 K.

Source of material

The title compound was prepared by the hydrocarbylation of theophylline (1.8 g, 10 mmol) and bromoacetic acid (9 mmol, 1.25 g) in the presence of tetrabutylammonium bromide catalyst (0.3 g). The reaction was carried out in a 630 W microwave oven for 1 min. Single crystals were obtained by recrystallization from ethanol solution.

Discussion

Xanthine derivatives are the naturally occurring drugs which find use as central nervous system stimulants. Caffeine, theophylline and theobromine are methyl derivatives of xanthine. Chemically theophylline is 1,3-dimethyl xanthine; caffeine – 1,3,7-trimethyl xanthine; theobromine – 3,7-dimethyl xanthine. Recently, more and more attention has been paid on the three alkaloid owing to their significant physiological effects, such as strong diuresis, cardiac stimulation as well as arterial dilation and are useful products in the food and pharmaceutical industries [1-3]. This has stimulated our interest in its derivatives and a derivative of theobromine, ethyl theobromineacetate [4]. To extend this research, we have synthesized a derivative of theophylline, theophylline-7-yl acetic acid, and determined its crystal structure.

The acetic part (C8/C9/O3/O4) and the theophylline heterocycle (C1/C2/C3/C4/C5/N1/N2/N3/N4) are each almost planar (figure, top). The dihedral angle between the above planes is 75.09(8)°. Moreover, the C—N bond lengths in the theophylline heterocycle range from 1.327(3) Å to 1.408(3) Å, which are shorter than a C—N single bond length (ca 1.443 Å [5], but longer than a typical C=N bond length (ca 1.269 Å), indicating the electron delocalization. One distinct hydrogen bond occurs in the crystal structure: adjacent molecules are linked by the intermolecular O3–H3···N4(x+½,–y+½,z+½) bond leading to chains along [101] direction (figure, bottom).

Table 1. Data collection and handling.

Crystal:	colorless block, size 0.09 × 0.15 × 0.16 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	1.29 cm^{-1}
Diffractometer, scan mode:	Bruker SMART APEX CCD, φ/ω
$2\theta_{max}$:	50.54°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	5068, 1788
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 1458
$N(param)_{refined}$:	157
Programs:	SHELXS-97 [6], SHELXL-97 [7]

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

Atom	Site	x	y	z	U_{iso}
H(3)	4*e*	1.0578	0.3555	0.4174	0.057
H(5)	4*e*	0.6155	0.2763	0.1198	0.040
H(6A)	4*e*	1.3392	0.1907	0.0482	0.064
H(6B)	4*e*	1.3268	0.3836	0.0956	0.064
H(6C)	4*e*	1.3191	0.3698	–0.0133	0.064
H(7A)	4*e*	0.8122	0.2472	–0.1885	0.061
H(7B)	4*e*	0.7750	0.0570	–0.1464	0.061
H(7C)	4*e*	0.9140	0.0780	–0.1911	0.061
H(8A)	4*e*	0.7543	0.4272	0.2624	0.038
H(8B)	4*e*	0.8849	0.5358	0.2360	0.038

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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(1)	4*e*	1.1383(2)	0.1974(3)	–0.1195(1)	0.045(1)	0.061(1)	0.034(1)	0.0012(9)	0.0178(9)	–0.0040(9)
O(2)	4*e*	1.1413(2)	0.4062(3)	0.1791(1)	0.032(1)	0.055(1)	0.032(1)	–0.0056(9)	–0.0010(8)	–0.0054(9)
O(3)	4*e*	0.9990(2)	0.4127(2)	0.3812(1)	0.035(1)	0.044(1)	0.031(1)	0.0048(8)	–0.0059(8)	–0.0024(8)
O(4)	4*e*	0.9641(2)	0.1406(3)	0.3077(1)	0.050(1)	0.038(1)	0.039(1)	0.0059(9)	–0.0029(9)	–0.0003(9)
N(1)	4*e*	1.1401(2)	0.2876(3)	0.0313(1)	0.028(1)	0.039(1)	0.030(1)	0.0015(9)	0.0054(9)	0.0027(9)
N(2)	4*e*	0.9283(2)	0.1936(3)	–0.0642(1)	0.035(1)	0.039(1)	0.024(1)	0.0004(9)	0.0031(9)	–0.0003(9)
N(3)	4*e*	0.8236(2)	0.3275(3)	0.1486(1)	0.026(1)	0.041(1)	0.022(1)	–0.0003(9)	0.0030(9)	0.0008(9)
N(4)	4*e*	0.7160(2)	0.2160(3)	0.0123(1)	0.028(1)	0.044(1)	0.026(1)	–0.0024(9)	–0.0005(9)	0.004(1)
C(1)	4*e*	1.0724(3)	0.2243(3)	–0.0551(2)	0.038(1)	0.032(1)	0.025(1)	0.002(1)	0.007(1)	0.003(1)
C(2)	4*e*	1.0750(3)	0.3386(3)	0.1087(2)	0.031(1)	0.032(1)	0.022(1)	0.001(1)	–0.000(1)	0.004(1)
C(3)	4*e*	0.9267(2)	0.3014(3)	0.0920(2)	0.026(1)	0.033(1)	0.023(1)	0.000(1)	0.002(1)	0.003(1)
C(4)	4*e*	0.8576(2)	0.2344(3)	0.0096(2)	0.028(1)	0.029(1)	0.023(1)	0.001(1)	0.001(1)	0.005(1)
C(5)	4*e*	0.7020(3)	0.2737(4)	0.0976(2)	0.025(1)	0.048(2)	0.026(1)	–0.001(1)	0.001(1)	0.005(1)
C(6)	4*e*	1.2947(3)	0.3099(4)	0.0413(2)	0.027(1)	0.056(2)	0.045(2)	–0.002(1)	0.008(1)	0.003(1)
C(7)	4*e*	0.8507(3)	0.1393(4)	–0.1554(2)	0.048(2)	0.049(2)	0.023(1)	–0.002(1)	–0.001(1)	–0.008(1)
C(8)	4*e*	0.8453(3)	0.4134(4)	0.2409(2)	0.030(1)	0.041(2)	0.023(1)	0.003(1)	0.005(1)	–0.000(1)
C(9)	4*e*	0.9433(2)	0.3026(4)	0.3124(2)	0.025(1)	0.039(2)	0.022(1)	0.001(1)	0.006(1)	–0.001(1)

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