Crystal structure of bis(8-chloro-5-(4-methylpiperazinium-1-yl)pyrido-[2,3-*b*][1,5]benzoxazepine) fumarate – fumaric acid solvate (1:1), $(C_{17}H_{18}ClN_4O)_2(C_4H_2O_4) \cdot C_4H_4O_4$

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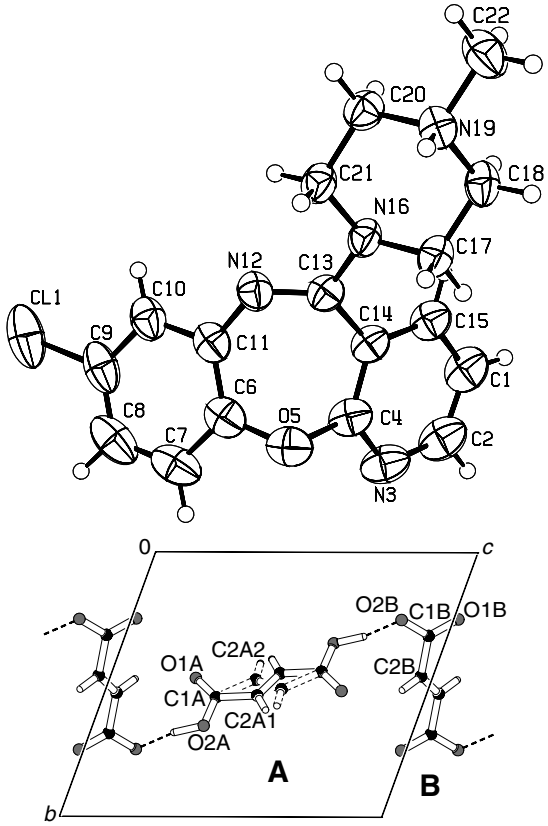
Received February 22, 2004, accepted and available on-line April 9, 2004; CCDC no. 1267/1256



Abstract

$C_{42}H_{42}Cl_2N_8O_{10}$, triclinic, $P\bar{1}$ (no. 2), a = 9.625(1) Å, b = 9.929(3) Å, c = 11.860(2) Å, α = 108.12(2)°, β = 73.24(1)°, γ = 87.38(1)°, V = 1019.9 Å^3, Z = 1, $R_{gt}(F)$ = 0.043, $wR_{ref}(F^2)$ = 0.131, T = 293 K.

Source of material

The compound was synthesized according to methods previously described [1]. Crystals were obtained by slow evaporation of a methanol solution.

Experimental details

The fumaric acid molecule is disordered, mainly the C2A atom. Two positions, C2A1 and C2A2, were refined with the sum of their respective site occupation factors (*s.o.f.*) restrained to 1.0, and their U_{ij} equated. H19, HO2A and H2B were located by Fourier difference synthesis. Only HO2A was included in the refinement. All other H atoms were restrained (included as riding atoms), with isotropic temperature parameters fixed at 1.2 U_{eq} of the parent atom (1.5 U_{eq} for methyl). In the final cycles of refinement, the position of atom C2A of the fumaric acid molecule (A) was split into two sites, C2A1 and C2A2, with occupation factors of 0.56 and 0.44, respectively (figure, bottom). The introduction of this disordered distribution improved the residual densities in the final difference map and also the conventional R and $wR(F^2)$ values. No significant electron density peak was found near O2B.

Discussion

The titled compound, a fumarate salt of 8-chloro-5-(4-methylpiperazin-1-yl)pyrido[2,3-*b*][1,5]benzoxazepine [2,3] also called JL13 was prepared as part of our study of dopamine receptors and related binding sites implicated in schizophrenia [1,4]. Extensive investigations have revealed a very promising antipsychotic profile in several preclinical models [5].

The oxazepine ring has a boat conformation where the four C atoms of the outer ring junction are almost coplanar: the maximum deviation from their mean plane is 0.022(1) Å (cf. JL13: 0.021(1) Å [2]). The deviation of the *'prow of the boat'*, viz. O5, is –0.615(3) Å, and those of N12 and C13 (*'the stern'*) –0.629(4) Å and –0.699(4) Å, respectively. The corresponding deviations in JL13 are larger: –0.668(1) Å, –0.667(1) Å and –0.762(1) Å, respectively [2]. The distances between the methylpiperazine atom N19 and the centres of the two aromatic rings are 7.545(4) Å and 5.958(4) Å, respectively (7.758(2) Å and 6.154(2) Å for JL13 [2]). The dihedral angle between the benzene and pyridine rings is 122.49(14)° (113,99(7)° for JL13 [2]). The torsion angle N12–C13–N16–C17 (142.8(2)°) is smaller than the equivalent one in JL13 (149.35(13)° [2]). The tetrahedral conformation of N19 is similar in both structures: in the fumarate salt, the sum of the three C–N19–C angles is equal to 331.5(1)°, in comparison with 332.05(7)° for JL13. The conformation around N16 is more tetrahedral in the salt than in JL13, with the sums of the three external angles around N16 equal to 346.6(1)° and 352.91(6)°, respectively.

The centres of symmetry of the fumaric acid molecules coincide respectively with the 1/2,1/2,0 and the 1/2,1/2,1/2 sites. So the asymmetric part of the unit cell contains three residues: the 8-chloro-5-(4-methylpiperazinium-1-yl)pyrido[2,3-*b*][1,5]benzoxazepine molecular ion with a protonated N19$^+$ amine, half a fumaric acid molecule (A) and half a fumarate moiety (B) with a COO^- group.

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The cohesion of the crystal is the result of van der Waals interactions and of two hydrogen bonds: $N19^+$–H19···O2B^{i} and O2A–HO2A···O2B^{ii} [codes: (i) x,–1+y,z; (ii) 1–x,1–y,1–z], where the distances N···O and O···O are 2.749(3) Å and 2.555(3) Å, and the angles N–H–O and O–H–O, 170° and 168(3)°, respectively.

Table 1. Data collection and handling.

Crystal:	colorless prism, size 0.34 × 0.53 × 0.53 mm
Wavelength:	Cu K_α radiation (1.54180 Å)
μ:	20.30 cm^{-1}
Diffractometer, scan mode:	Stoe-Siemens AED, ω
$2\theta_{max}$:	125.02°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	3023, 2823
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2301
$N(param)_{refined}$:	289
Programs:	SHELXS-97 [6],SHELXL-97 [7], ORTEP-III [8]

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

Atom	Site	Occ.	x	y	z	U_{iso}
H(1)	2*i*		0.1500	0.4929	0.2384	0.080
H(2)	2*i*		–0.0847	0.4387	0.2779	0.088
H(7)	2*i*		–0.2605	0.1843	0.6480	0.081
H(8)	2*i*		–0.2730	0.2488	0.8557	0.089
H(10)	2*i*		0.1598	0.2646	0.7637	0.069
H(15)	2*i*		0.3127	0.3813	0.3031	0.068
H(171)	2*i*		0.3573	0.1406	0.1855	0.059
H(172)	2*i*		0.4054	–0.0119	0.1878	0.059
H(181)	2*i*		0.6009	0.0516	0.0527	0.060
H(182)	2*i*		0.5973	0.1927	0.1617	0.060
H(19)	2*i*		0.6550	–0.0766	0.1661	0.056
H(201)	2*i*		0.6709	0.1752	0.3411	0.060
H(202)	2*i*		0.7128	0.0220	0.3448	0.060
H(211)	2*i*		0.4727	–0.0210	0.3757	0.058
H(212)	2*i*		0.4708	0.1253	0.4778	0.058
H(221)	2*i*		0.8919	–0.0370	0.1434	0.104
H(222)	2*i*		0.8501	0.1090	0.1276	0.104
H(223)	2*i*		0.8475	–0.0359	0.0265	0.104
H(2A1)	2*i*	0.557	0.6205	0.4043	0.4814	0.062
H(2A2)	2*i*	0.443	0.3627	0.5798	0.5494	0.062
H(O2A)	2*i*		0.446(4)	0.318(4)	0.740(4)	0.094
H(2B)	2*i*		0.5724	0.4805	0.0792	0.064

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

Atom	Site	Occ.	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	2*i*		0.1220(4)	0.4276(3)	0.2794(3)	0.083(2)	0.048(2)	0.082(2)	–0.003(1)	–0.036(2)	0.032(1)
C(2)	2*i*		–0.0202(4)	0.3935(3)	0.3047(3)	0.080(2)	0.061(2)	0.092(2)	0.003(2)	–0.044(2)	0.032(2)
N(3)	2*i*		–0.0746(3)	0.3005(2)	0.3648(2)	0.063(1)	0.055(1)	0.091(2)	–0.001(1)	–0.039(1)	0.025(1)
C(4)	2*i*		0.0177(3)	0.2389(3)	0.3991(3)	0.055(2)	0.039(1)	0.068(2)	–0.003(1)	–0.026(1)	0.016(1)
O(5)	2*i*		–0.0410(2)	0.1397(2)	0.4577(2)	0.057(1)	0.047(1)	0.083(1)	–0.0090(8)	–0.026(1)	0.0256(9)
C(6)	2*i*		–0.0434(3)	0.1842(3)	0.5825(3)	0.052(2)	0.039(1)	0.070(2)	–0.002(1)	–0.013(1)	0.023(1)
C(7)	2*i*		–0.1765(3)	0.2000(3)	0.6711(3)	0.047(2)	0.049(2)	0.100(3)	–0.003(1)	–0.009(2)	0.028(2)
C(8)	2*i*		–0.1838(3)	0.2394(3)	0.7943(3)	0.057(2)	0.049(2)	0.094(3)	0.003(1)	0.013(2)	0.029(2)
C(9)	2*i*		–0.0572(3)	0.2654(3)	0.8277(3)	0.073(2)	0.044(1)	0.062(2)	0.006(1)	0.008(2)	0.025(1)
C(10)	2*i*		0.0765(3)	0.2479(3)	0.7398(2)	0.058(2)	0.054(2)	0.057(2)	0.001(1)	–0.006(1)	0.027(1)
C(11)	2*i*		0.0863(3)	0.2045(2)	0.6136(2)	0.048(2)	0.040(1)	0.058(2)	0.002(1)	–0.008(1)	0.022(1)
N(12)	2*i*		0.2243(2)	0.1684(2)	0.5277(2)	0.045(1)	0.050(1)	0.047(1)	0.0022(9)	–0.0071(9)	0.0205(9)
C(13)	2*i*		0.2582(3)	0.1882(2)	0.4213(2)	0.045(1)	0.040(1)	0.049(1)	–0.001(1)	–0.015(1)	0.015(1)
C(14)	2*i*		0.1643(3)	0.2635(2)	0.3778(2)	0.052(2)	0.038(1)	0.054(1)	–0.001(1)	–0.021(1)	0.016(1)
C(15)	2*i*		0.2166(3)	0.3625(3)	0.3167(3)	0.063(2)	0.047(1)	0.066(2)	–0.007(1)	–0.027(1)	0.023(1)
N(16)	2*i*		0.3981(2)	0.1478(2)	0.3440(2)	0.047(1)	0.052(1)	0.038(1)	0.0047(9)	–0.0125(9)	0.0170(9)
C(17)	2*i*		0.4234(3)	0.0868(3)	0.2097(2)	0.056(2)	0.049(1)	0.042(1)	0.000(1)	–0.017(1)	0.016(1)
C(18)	2*i*		0.5802(3)	0.0937(3)	0.1425(2)	0.060(2)	0.047(1)	0.043(1)	–0.001(1)	–0.011(1)	0.021(1)
N(19)	2*i*		0.6743(2)	0.0152(2)	0.1837(2)	0.049(1)	0.039(1)	0.046(1)	–0.0004(8)	–0.0071(9)	0.0155(8)
C(20)	2*i*		0.6490(3)	0.0777(3)	0.3203(2)	0.049(1)	0.051(1)	0.047(1)	0.001(1)	–0.016(1)	0.013(1)
C(21)	2*i*		0.4913(3)	0.0770(3)	0.3887(2)	0.049(1)	0.054(1)	0.042(1)	0.005(1)	–0.013(1)	0.018(1)
C(22)	2*i*		0.8296(3)	0.0126(3)	0.1142(3)	0.053(2)	0.075(2)	0.068(2)	0.002(1)	0.003(1)	0.030(2)
Cl(1)	2*i*		–0.0660(1)	0.32060(9)	0.98425(7)	0.1189(8)	0.0742(5)	0.0588(5)	0.0055(5)	0.0158(4)	0.0264(4)
C(1A)	2*i*		0.4334(5)	0.4513(4)	0.6491(3)	0.108(3)	0.089(2)	0.045(2)	–0.049(2)	–0.032(2)	0.034(2)
C(2A1)	2*i*	0.557(5)	0.5276(6)	0.4580(6)	0.5231(5)	0.064(3)	0.045(2)	0.048(3)	0.001(2)	–0.019(3)	0.018(2)
C(2A2)	2*i*	0.443	0.4408(9)	0.5177(7)	0.5452(7)	0.064(3)	0.045(2)	0.048(3)	0.001(2)	–0.019(3)	0.018(2)
O(1A)	2*i*		0.3350(3)	0.5238(3)	0.7329(2)	0.109(2)	0.093(2)	0.082(2)	0.002(2)	–0.038(2)	0.047(1)
O(2A)	2*i*		0.4979(2)	0.3437(3)	0.6555(2)	0.079(2)	0.087(2)	0.053(1)	–0.003(1)	–0.007(1)	0.016(1)
C(1B)	2*i*		0.5731(3)	0.6854(3)	0.0589(2)	0.056(2)	0.039(1)	0.050(2)	0.001(1)	–0.014(1)	0.014(1)
C(2B)	2*i*		0.5380(3)	0.5326(3)	0.0372(2)	0.069(2)	0.043(1)	0.046(1)	0.004(1)	–0.019(1)	0.015(1)
O(1B)	2*i*		0.5707(3)	0.7481(2)	–0.0145(2)	0.120(2)	0.051(1)	0.062(1)	–0.009(1)	–0.036(1)	0.027(1)
O(2B)	2*i*		0.6028(2)	0.7453(2)	0.1608(2)	0.092(1)	0.044(1)	0.060(1)	–0.0061(9)	–0.036(1)	0.0168(8)

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