Crystal structure of desvenlafaxinium 3,5-dinitrobenzoate 3,5-dinitrobenzoic acid monohydrate, $C_{30}H_{35}N_5O_{15}$

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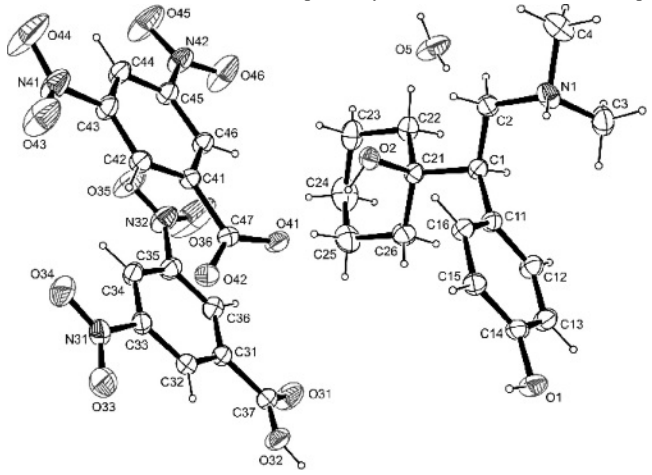

Abstract

$C_{30}H_{35}N_5O_{15}$, triclinic, $P\overline{1}$ (no. 2), a = 10.5412(2) Å, b = 12.6593(3) Å, c = 13.2189(3) Å, α = 68.273(1)°, β = 79.846(1)°, γ = 88.627(1)°, V = 1611.4 Å^3, Z = 2, $R_{gt}(F)$ = 0.0432, $wR_{ref}(F^2)$ = 0.1180, T = 200 K.

Table 1. Data collection and handling.

Crystal:	yellow blocks, size 0.16×0.25×0.41 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	1.18 cm^{-1}
Diffractometer, scan mode:	Bruker APEX-II CCD, φ and ω
$2\theta_{max}$:	56.88°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	43643, 8086
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 7072
$N(param)_{refined}$:	461
Programs:	SHELX [12], ORTEP-3 [15], MERCURY [16], PLATON [17]

Source of material

Desvenlafaxine succinate was obtained as a gift sample from R. L. Fine Chem, Bengaluru, India. A solution of desvenlafaxine succinate in water was treated with ammonium hydroxide solution till a pH > 7 was reached upon which a white precipitate of desvenlafaxine was obtained. The precipitate was filtered and dried in open air overnight. It was used for the preparation of the dinitrobenzoate salt without further purification. Desvenlafaxine (200 mg, 0.76 mmol) and 3,5-dinitrobenzoic acid (161 mg, 0.76 mmol) were dissolved in hot methanol and stirred at 333 K for 30 minutes. The resulting solution was allowed to cool slowly to room temperature. The salt obtained was filtered and dried in a vacuum desiccator over phosphorous pentoxide. The resulting compound was recrystallized from acetonitrile by slow evaporation.

Experimental details

Carbon-bound H atoms were placed in calculated positions (C–H 0.95 Å, C–H 0.99 Å for methylene groups and C–H 1.00 Å for methine groups) and were included in the refinement in the riding model approximation, with U_{iso}(H) set to 1.2U_{eq}(C). The H atoms of the methyl groups were allowed to rotate with a fixed angle around the C–C bond to best fit the experimental electron density (HFIX 137 in the SHELX program suite [12]), with U_{iso}(H) set to 1.5U_{eq}(C). Both nitrogen-bound H atoms were located on a difference Fourier map and refined freely.

Discussion

Desvenlafaxine – also known as *O*-desmethylvenlafaxine – is an antidepressant of the serotonin-norepinephrine re-uptake inhibitor class [1]. Desvenlafaxine is a synthetic form of the major active metabolite of venlafaxine and is being investigated as the first non-hormonal based treatment for menopause. It is a racemic mixture and is reported to exist in four crystalline polymorphs [2]. Furthermore the crystal structure of venlafaxine hydrochloride [3], a monoclinic polymorph of venlafaxine hydrochloride [4], venlafaxine itself [5], desvenlafaxine succinate monohydrate [6] and two polytypes of desvenlafaxine succinate monohydrate [7] have been reported. The crystal structure of a ternary complex, 4-(2-pyridyl)pyridinium-3,5-dinitrobenzoate-3,5-dinitrobenzoic acid (1/1/1), is apparent in the literature [8], and an orthorhombic-to-monoclinic temperature-dependent phase transition of hexa-methylenetetraminium-3,5-dinitrobenzoate-3,5-dinitrobenzoic acid monohydrate in the solid state has been described [9]. In the crystal, a molecule of water is present next to one additional molecule of the – non-dissociated – carboxylic acid. While the least-squares planes defined by the atoms of the nitro groups of the deprotonated carboxylic acid enclose angles of 5.8(2)° and 9.8(2)° with the plane defined by the carbon atoms of the aromatic system they are bonded to, the least-squares plane defined by the atoms of the carboxylate group intersect with the aromat's plane at an angle of 13.88(14)°. The respective values for the co-crystallized carboxylic acid are found at 4.9(2)° and 7.25(16)° for the nitro groups and 11.12(16)° for the least-squares plane defined by the non-hydrogen atoms of the carboxylic acid group on the one hand and the plane defined by the carbon atoms of the aromatic system they are bonded to on the other hand. According to a puckering analysis, the saturated six-membered ring adopts a $^4C_1$ conformation ($^{C24}C_{C21}$) [10, 11]. In the crystal, hydrogen bonds of the N–H···O as well as the O–H···O type are ob-

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served. In total, the different moieties of the title compound are connected to a three-dimensional network. The shortest inter-centroid distance between two centers of gravity was measured at 4.2942(8) Å and is apparent between the aromatic system of the cation as well as the phenyl ring of the deprotonated carboxylic acid.

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

Atom	Site	*x*	*y*	*z*	U_{iso}
H(1A)	2*i*	0.089(2)	–0.3163(7)	0.750(1)	0.045
H(2)	2*i*	0.152(2)	0.215(2)	0.4724(9)	0.037
H(5A)	2*i*	0.0105	0.6607	0.6003	0.062(6)
H(5B)	2*i*	0.0585	0.5582	0.6721	0.13(1)
H(32A)	2*i*	0.684(2)	–0.0446(9)	0.539(2)	0.047
H(1B)	2*i*	–0.2438	0.0733	0.7356	0.033
H(1)	2*i*	0.0131	0.1925	0.7638	0.025
H(2A)	2*i*	–0.1396	0.2927	0.6681	0.029
H(2B)	2*i*	–0.1323	0.2160	0.5949	0.029
H(3A)	2*i*	–0.1580	0.0608	0.8846	0.056
H(3B)	2*i*	–0.3116	0.0637	0.9144	0.056
H(3C)	2*i*	–0.2236	0.1762	0.8842	0.056
H(4A)	2*i*	–0.3668	0.2235	0.6488	0.060
H(4B)	2*i*	–0.3672	0.2647	0.7497	0.060
H(4C)	2*i*	–0.4372	0.1457	0.7709	0.060
H(12)	2*i*	0.0824	0.0229	0.8699	0.031
H(13)	2*i*	0.1210	–0.1694	0.9150	0.033
H(15)	2*i*	0.0249	–0.1523	0.6258	0.028
H(16)	2*i*	–0.0222	0.0386	0.5852	0.027
H(22A)	2*i*	0.0181	0.4066	0.5677	0.032
H(22B)	2*i*	0.1031	0.3836	0.6622	0.032
H(23A)	2*i*	0.2034	0.4588	0.4293	0.043
H(23B)	2*i*	0.2037	0.5339	0.5036	0.043
H(24A)	2*i*	0.4112	0.4611	0.4696	0.055
H(24B)	2*i*	0.3544	0.4177	0.5996	0.055
H(25A)	2*i*	0.4380	0.2622	0.5576	0.047
H(25B)	2*i*	0.3519	0.2864	0.4636	0.047
H(26A)	2*i*	0.2540	0.2093	0.6969	0.035
H(26B)	2*i*	0.2529	0.1349	0.6220	0.035
H(32)	2*i*	0.6089	0.0398	0.2943	0.030
H(34)	2*i*	0.5300	0.3479	0.0764	0.033
H(36)	2*i*	0.6207	0.3212	0.3717	0.033
H(42)	2*i*	0.2171	0.1922	0.0669	0.028
H(44)	2*i*	0.1504	0.5309	–0.0396	0.032
H(46)	2*i*	0.2429	0.3677	0.2654	0.027

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)	2*i*	0.10008(9)	–0.29271(7)	0.80498(8)	0.0373(5)	0.0191(4)	0.0340(5)	0.0068(3)	–0.0103(4)	–0.0081(4)
O(2)	2*i*	0.09025(8)	0.24892(8)	0.49726(7)	0.0269(4)	0.0299(4)	0.0201(4)	0.0034(3)	–0.0057(3)	–0.0131(3)
O(5)	2*i*	0.0643(1)	0.6290(1)	0.6475(1)	0.0872(9)	0.0376(6)	0.0473(7)	0.0267(6)	–0.0370(7)	–0.0219(5)
O(31)	2*i*	0.6965(1)	0.1455(1)	0.51442(9)	0.0686(8)	0.0393(6)	0.0344(5)	0.0086(5)	–0.0260(5)	–0.0151(5)
O(32)	2*i*	0.6522(1)	–0.00849(8)	0.47962(8)	0.0393(5)	0.0297(5)	0.0262(5)	0.0088(4)	–0.0144(4)	–0.0073(4)
O(33)	2*i*	0.5810(1)	0.0353(1)	0.11773(9)	0.0591(7)	0.0401(6)	0.0361(6)	0.0095(5)	–0.0079(5)	–0.0208(5)
O(34)	2*i*	0.5132(1)	0.1931(1)	0.01214(9)	0.0600(7)	0.0536(7)	0.0267(5)	0.0119(5)	–0.0167(5)	–0.0170(5)
O(35)	2*i*	0.5119(2)	0.5239(1)	0.1092(1)	0.087(1)	0.0310(6)	0.0452(7)	0.0101(6)	–0.0294(6)	–0.0024(5)
O(36)	2*i*	0.5731(3)	0.5133(1)	0.2576(2)	0.217(2)	0.0364(7)	0.085(1)	0.027(1)	–0.093(1)	–0.0300(8)
O(41)	2*i*	0.26605(9)	0.15722(8)	0.36248(7)	0.0382(5)	0.0253(4)	0.0228(4)	0.0107(4)	–0.0123(4)	–0.0096(3)
O(42)	2*i*	0.29742(9)	0.07309(7)	0.23837(7)	0.0317(4)	0.0185(4)	0.0276(4)	0.0028(3)	–0.0040(3)	–0.0090(3)
O(43)	2*i*	0.1457(2)	0.2632(1)	–0.1094(1)	0.113(1)	0.0403(6)	0.0436(7)	0.0149(7)	–0.0412(7)	–0.0252(5)
O(44)	2*i*	0.1064(2)	0.4406(1)	–0.1631(1)	0.172(2)	0.0444(7)	0.0480(8)	0.0339(9)	–0.070(1)	–0.0192(6)
O(45)	2*i*	0.1880(2)	0.65744(9)	0.0541(1)	0.136(1)	0.0210(5)	0.0475(7)	0.0152(6)	–0.0450(8)	–0.0094(5)
O(46)	2*i*	0.2062(2)	0.5687(1)	0.2223(1)	0.136(1)	0.0280(5)	0.0349(6)	0.0147(7)	–0.0335(7)	–0.0179(5)
N(1)	2*i*	–0.2408(1)	0.13989(9)	0.74965(9)	0.0285(5)	0.0218(5)	0.0330(6)	–0.0015(4)	0.0040(4)	–0.0146(4)
N(31)	2*i*	0.5531(1)	0.1347(1)	0.09587(9)	0.0335(6)	0.0389(6)	0.0235(5)	0.0039(5)	–0.0031(4)	–0.0138(5)
N(32)	2*i*	0.5504(1)	0.4709(1)	0.1944(1)	0.0586(8)	0.0261(6)	0.0375(7)	0.0009(5)	–0.0156(6)	–0.0063(5)
N(41)	2*i*	0.1418(2)	0.3538(1)	–0.0976(1)	0.0737(9)	0.0341(6)	0.0277(6)	0.0101(6)	–0.0247(6)	–0.0144(5)
N(42)	2*i*	0.1961(1)	0.57035(9)	0.1322(1)	0.0567(7)	0.0193(5)	0.0286(6)	0.0060(5)	–0.0150(5)	–0.0091(4)
C(1)	2*i*	0.0050(1)	0.17722(9)	0.69615(9)	0.0268(5)	0.0189(5)	0.0191(5)	0.0022(4)	–0.0043(4)	–0.0084(4)
C(2)	2*i*	–0.1289(1)	0.2141(1)	0.6699(1)	0.0253(5)	0.0191(5)	0.0260(6)	0.0011(4)	–0.0013(4)	–0.0074(4)
C(3)	2*i*	–0.2328(2)	0.1074(1)	0.8683(1)	0.0453(8)	0.0325(7)	0.0291(7)	0.0010(6)	0.0073(6)	–0.0109(6)
C(4)	2*i*	–0.3636(1)	0.1985(1)	0.7279(1)	0.0264(6)	0.0439(8)	0.0531(9)	0.0028(6)	–0.0002(6)	–0.0253(7)
C(11)	2*i*	0.0257(1)	0.0515(1)	0.72285(9)	0.0249(5)	0.0191(5)	0.0212(5)	0.0024(4)	–0.0037(4)	–0.0072(4)
C(12)	2*i*	0.0690(1)	–0.0127(1)	0.8205(1)	0.0330(6)	0.0244(6)	0.0231(5)	0.0031(5)	–0.0081(5)	–0.0097(5)
C(13)	2*i*	0.0931(1)	–0.1272(1)	0.8474(1)	0.0314(6)	0.0247(6)	0.0243(6)	0.0047(5)	–0.0090(5)	–0.0055(5)
C(14)	2*i*	0.0762(1)	–0.1798(1)	0.7750(1)	0.0214(5)	0.0187(5)	0.0278(6)	0.0026(4)	–0.0028(4)	–0.0060(4)
C(15)	2*i*	0.0350(1)	–0.1171(1)	0.6764(1)	0.0249(5)	0.0203(5)	0.0248(6)	0.0013(4)	–0.0041(4)	–0.0092(4)
C(16)	2*i*	0.0083(1)	–0.0029(1)	0.6517(1)	0.0262(5)	0.0204(5)	0.0216(5)	0.0020(4)	–0.0060(4)	–0.0070(4)
C(21)	2*i*	0.1114(1)	0.2541(1)	0.60034(9)	0.0244(5)	0.0218(5)	0.0188(5)	0.0009(4)	–0.0049(4)	–0.0094(4)
C(22)	2*i*	0.1016(1)	0.3788(1)	0.5894(1)	0.0351(6)	0.0217(5)	0.0241(6)	–0.0030(5)	–0.0020(5)	–0.0101(5)
C(23)	2*i*	0.2112(2)	0.4557(1)	0.5038(1)	0.0451(8)	0.0294(7)	0.0310(7)	–0.0120(6)	0.0007(6)	–0.0110(5)
C(24)	2*i*	0.3426(2)	0.4126(2)	0.5289(1)	0.0392(8)	0.055(1)	0.0450(9)	–0.0208(7)	–0.0028(6)	–0.0214(7)
C(25)	2*i*	0.3541(1)	0.2899(1)	0.5369(1)	0.0241(6)	0.0568(9)	0.0387(8)	–0.0028(6)	–0.0064(5)	–0.0197(7)
C(26)	2*i*	0.2451(1)	0.2128(1)	0.6224(1)	0.0257(6)	0.0368(7)	0.0285(6)	0.0041(5)	–0.0091(5)	–0.0130(5)
C(31)	2*i*	0.6195(1)	0.1697(1)	0.3497(1)	0.0225(5)	0.0281(6)	0.0209(5)	0.0029(4)	–0.0039(4)	–0.0063(4)
C(32)	2*i*	0.6006(1)	0.1193(1)	0.2759(1)	0.0236(5)	0.0274(6)	0.0234(5)	0.0042(4)	–0.0031(4)	–0.0084(5)
C(33)	2*i*	0.5696(1)	0.1873(1)	0.1752(1)	0.0232(5)	0.0316(6)	0.0207(5)	0.0021(4)	–0.0022(4)	–0.0095(5)

Table 3. continued.

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(34)	2*i*	0.5527(1)	0.3028(1)	0.1455(1)	0.0258(6)	0.0300(6)	0.0210(5)	0.0009(5)	–0.0035(4)	–0.0037(5)
C(35)	2*i*	0.5708(1)	0.3490(1)	0.2218(1)	0.0297(6)	0.0243(6)	0.0265(6)	0.0001(5)	–0.0053(5)	–0.0048(5)
C(36)	2*i*	0.6060(1)	0.2859(1)	0.3225(1)	0.0286(6)	0.0286(6)	0.0248(6)	0.0003(5)	–0.0055(5)	–0.0089(5)
C(37)	2*i*	0.6596(1)	0.1007(1)	0.4577(1)	0.0275(6)	0.0318(6)	0.0230(6)	0.0062(5)	–0.0062(4)	–0.0090(5)
C(41)	2*i*	0.2354(1)	0.26323(9)	0.17994(9)	0.0216(5)	0.0187(5)	0.0206(5)	0.0015(4)	–0.0048(4)	–0.0068(4)
C(42)	2*i*	0.2108(1)	0.2608(1)	0.0808(1)	0.0276(5)	0.0209(5)	0.0222(5)	0.0022(4)	–0.0060(4)	–0.0094(4)
C(43)	2*i*	0.1771(1)	0.3595(1)	0.0030(1)	0.0365(6)	0.0253(6)	0.0197(5)	0.0033(5)	–0.0094(5)	–0.0088(5)
C(44)	2*i*	0.1717(1)	0.4634(1)	0.0158(1)	0.0370(6)	0.0215(5)	0.0212(5)	0.0041(5)	–0.0089(5)	–0.0055(4)
C(45)	2*i*	0.1994(1)	0.4624(1)	0.1143(1)	0.0333(6)	0.0178(5)	0.0226(5)	0.0027(4)	–0.0070(4)	–0.0080(4)
C(46)	2*i*	0.2282(1)	0.3650(1)	0.19754(9)	0.0285(6)	0.0205(5)	0.0200(5)	0.0022(4)	–0.0073(4)	–0.0077(4)
C(47)	2*i*	0.2684(1)	0.15432(9)	0.26752(9)	0.0206(5)	0.0185(5)	0.0219(5)	0.0017(4)	–0.0052(4)	–0.0064(4)

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