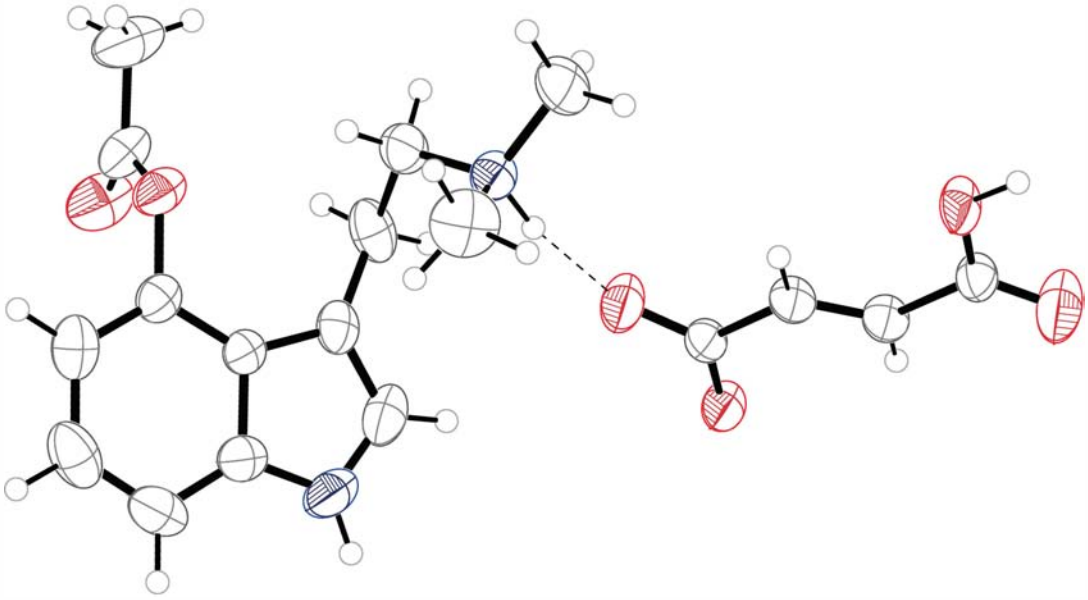

The Crystal Structure of 4-AcO-DMT Fumarate

Andrew R. Chadeayne,[a*] **James A. Golen**[b] and **David R. Manke**[b]

[a]CaaMTech, LLC, 58 East Sunset Way, suite 209, Issaquah, WA 98027

[b]Department of Chemistry and Biochemistry, University of Massachusetts Dartmouth, 285 Old Westport Road, North Dartmouth, MA 02747

*e-mail: andrew@caam.tech

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Introduction

There has been a recent increase in the study of psychedelic agents, as potential pharmaceuticals for the treatment of mood disorders.[1] 4-acetoxy-*N,N*-dimethyltryptamine, commonly 4-AcO-DMT or psilacetin, is the *O*-acetyl prodrug of psilocin. Psilocin is the primary metabolite of psilocybin, and the active component of hallucinogenic or "magic" mushrooms. Psilacetin also generates psilocin upon metabolism, but is easier to synthesize than psilocybin. Nichols first reported the synthesis of psilacetin in 1999,[2] and the compound is usually produced as the crystalline fumarate salt. Herein, we report the solid state structure of 4-acetoxy-*N,N*-dimethyltryptamine fumarate.

Structure Description

The molecular structure of the fumarate salt of psilacetin is shown in Figure 1. The asymmetric unit contains one 4-acetoxy-*N,N*-dimethyltryptammonium cation and one 3-carboxyacrylate anion. The indole of the cation is near planar with a mean deviation from planarity of 0.011 Å. The acetate unit is positioned in a perpendicular fashion, with the angle between the indole and acetate planes being 92.75(6)°. The singly protonated fumarate is in the *trans* configuration and is also nearly planar with a mean deviation from planarity of 0.053 Å. The ions are held together in the solid state through a series of hydrogen bonds (*vide infra*).

Table 1. Hydrogen-bond geometry for 4-AcO-DMT fumarate

D–H···*A*	*D*–H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*–H···*A* (°)
N1–H1···O4^{i}	0.86(3)	2.03(3)	2.87(1)	165(3)
O6–H6a···O4^{ii}	0.99(3)	1.56(3)	2.55(2)	178(2)
N2–H2···O3	0.90(2)	1.80(2)	2.69(2)	168(2)

(i) 1 – x, ½ + y, ½ – z; (ii) x, –1 + y, z

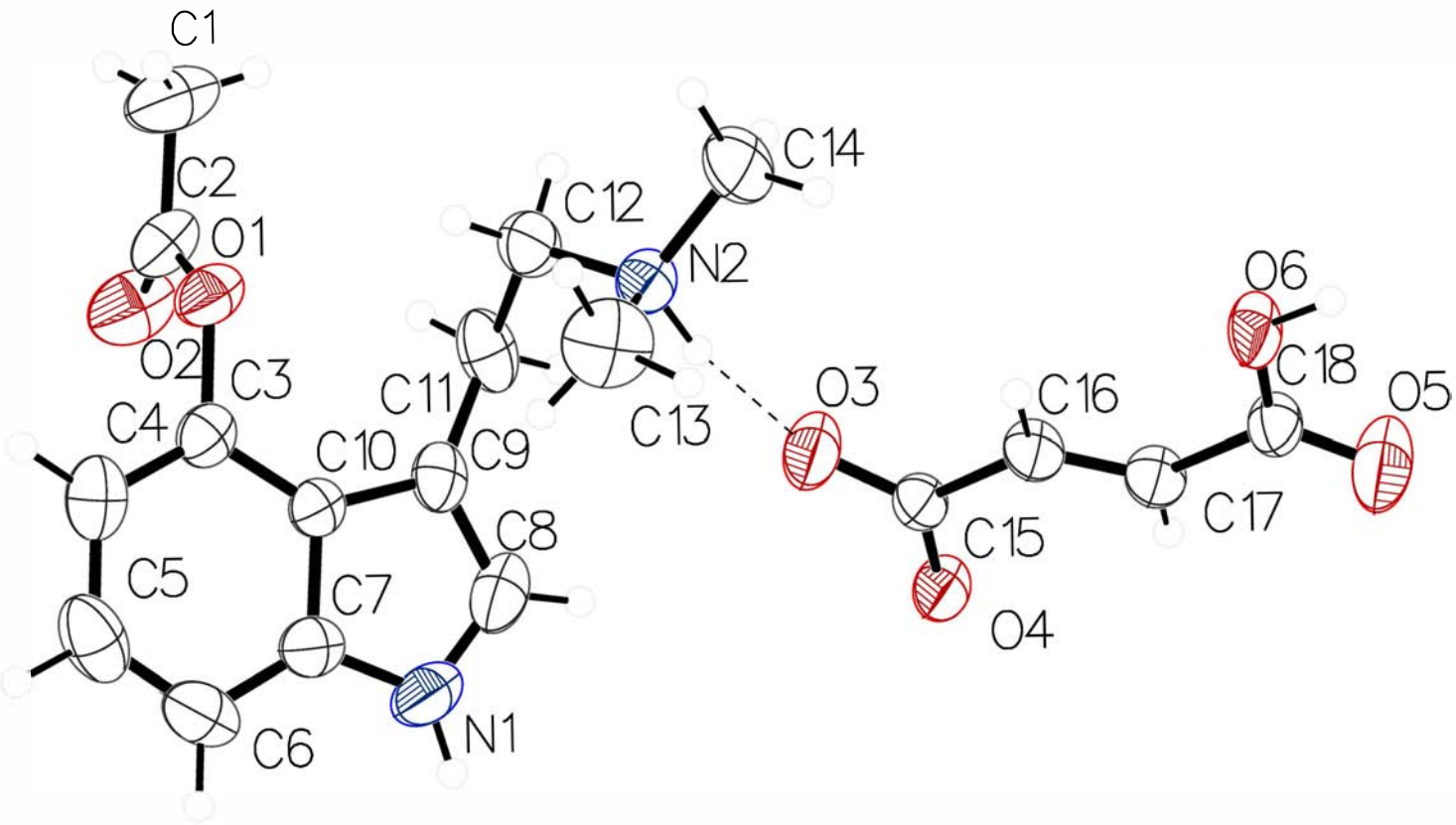

Figure 1. The molecular structure of 4-acetoxy-*N,N*-dimethyltryptamine fumarate, showing the atom labelling. Displacement ellipsoids are drawn at the 50% probability level. Hydrogen bonds are shown as dashed lines (see Table 1).

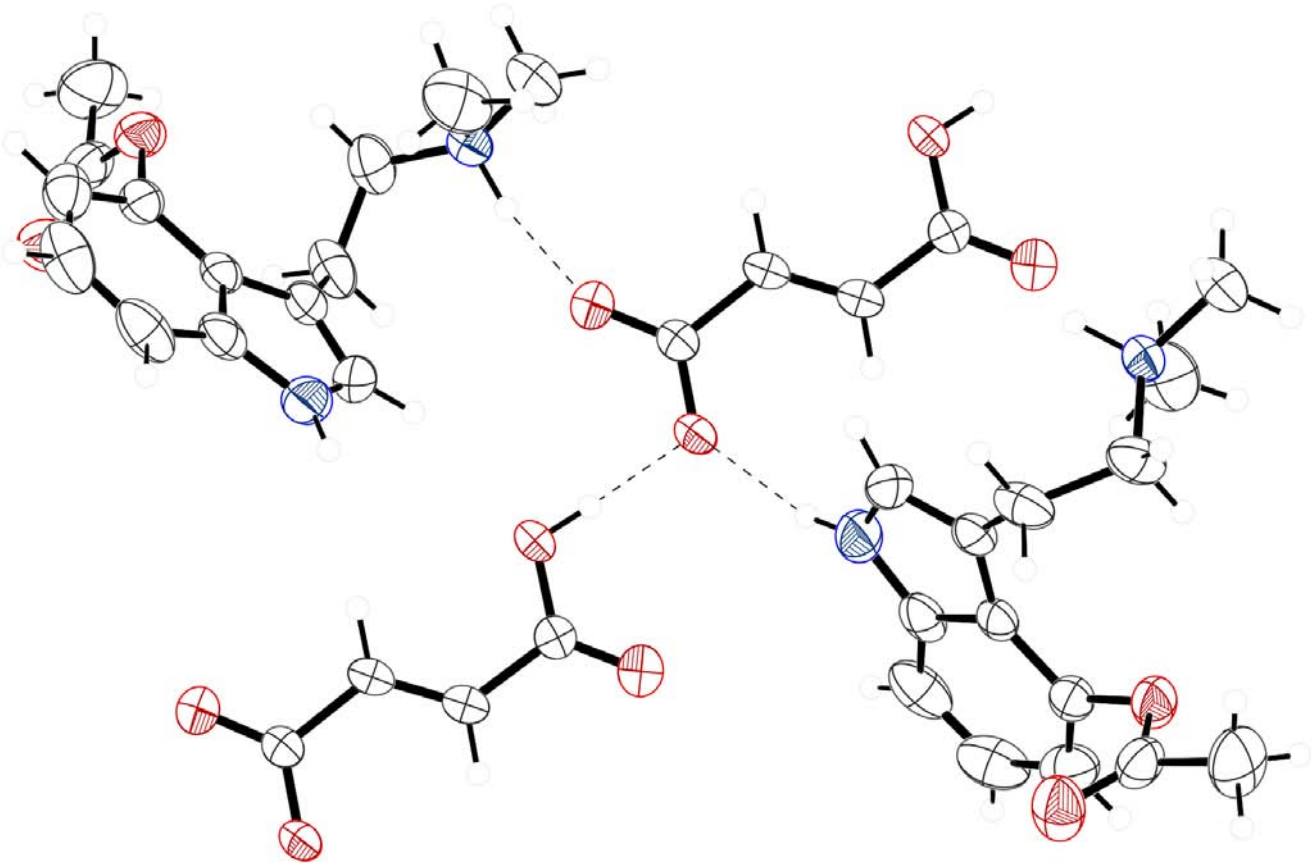

Figure 2. The hydrogen bonding of the fumarate anion in the structure of 4-acetoxy-*N*,*N*-dimethyltryptamine fumarate. The acetate end of the fumarate has three hydrogen bonds – one with an ammonium hydrogen, one with an indole hydrogen and one with the carboxylic acid
hydrogen of another fumarate.

Supramolecular features

The 4-acetoxy-*N*,*N*-dimethyltyptamine and fumarate ions are linked together into infinite chains along the [010] direction through N–H···O and O–H···O hydrogen bonds. One oxygen of the carboxylate on the 3-carboxyacrylate ion forms a hydrogen bond with the proton on the ammonium salt of a psilacetin molecule. The other oxygen of the carboxylate forms a hydrogen bond with an indole hydrogen, and also forms a hydrogen bond with the carboxylic acid of another fumarate ion (Figure 2). The packing of the compound is shown in Figure 3.

Related structures

The two most closely related structures reported are the naturally occurring hallucinogenic agents found in mushrooms: psilocybin[3] and psilocin[4]. The bond distances and angles observed in the dimethyltryptamine units of these two compounds and the structure reported here are nearly identical. In the psilocybin structure one of the phosphate protons is transferred to the dimethylamino nitrogen, producing an ammonium/phosphate zwitterion. The nature of the psilocin structure is not as clear, believed to exist as a statistical mixture of zwitterions and neutral molecules, with a proton involved in an intramolecular hydrogen bond between the hydroxide and the amine. The reported structure differs as it exists as an ion pair between the protonated ammonium salt and the singly deprotonated 3-carboxyacrylate.

Crystallization

A commercial sample (The Indole Shop) of 4-acetoxy-*N*,*N*-dimethyltryptamine fumarate was used for crystallization. Colorless crystals were grown by slow evaporation of an aqueous solution.

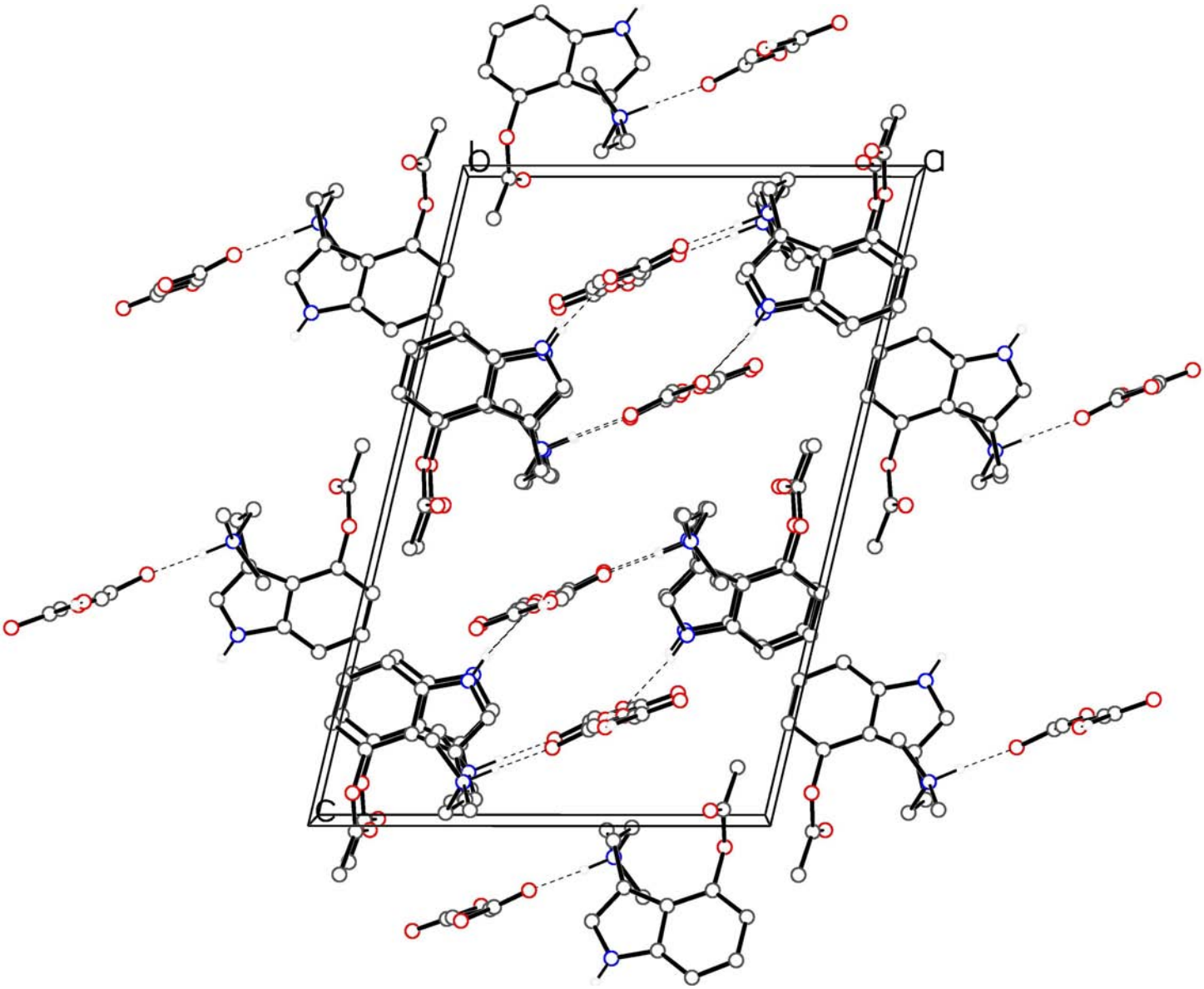

Figure 3. The crystal packing of 4-acetoxy-*N,N*-dimethyltryptamine fumarate, viewed along the b axis. The N–H···O and O–H···O hydrogen bonds are shown as dashed lines. Hydrogen atoms not involved in H-bonding have been removed for clarity.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. The structure solution was obtained by intrinsic phasing. All non-hydrogen atoms were refined anisotropically (*SHELXL*) by full-matrix least squares on F^2. Hydrogen atoms H1, H2 and H6a were found from Fourier difference maps and refined isotropically with 1.50 U_{eq} of parent N or O atoms. All other hydrogen atoms were placed in calculated positions with appropriate carbon-hydrogen bond lengths and: C–H(Ar) 0.930 Å, CH_2 0.970 Å and CH_3 0.960 Å and 1.20, 1.20 and 1.50 U_{eq} of parent C atoms.

Acknowledgements

We acknowledge support from the National Science Foundation (award No. CHE-1429086) that purchased the X-ray diffractometer.

Supplementary Material

CCDC 1897284 contains the supplementary crystallographic data for the compound. The data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retreiving/html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

Table 2. Crystal data and structure refinement for 4-AcO-DMT fumarate

Empirical formula	$C_{18}H_{22}N_2O_6$
Formula weight	362.37
Temperature (K)	296
Crystal system, space group	monoclinic, $P2_1/c$
a, *b*, *c* (Å)	13.023(1), 7.4823(6), 19.102(2)
α, *β*, *γ* (°)	90, 103.251(3), 90
V (Å^3)	1811.8(3)
Z	4
Radiation type	Mo *Kα* (λ = 0.71073)
μ (mm-1)	0.100
F(000)	768.0
Crystal size (mm^3)	0.27 × 0.22 × 0.20
Diffractometer	Bruker D8 Venture CMOS
Absorption correction	Multi-scan
Reflections collected	43099
Independent reflections	3320 [R_{int} = 0.0366, R_{sigma} = 0.0144]
Data/restraints/parameters	3320/0/251
Goodness-of-fit on F^2	1.037
Final R indexes [I ≥ 2σ (I)]	R_1 = 0.0419, wR_2 = 0.1024
Final R indexes [all data]	R_1 = 0.0522, wR_2 = 0.1118
Largest diff. peak/hole (e Å^{-3})	0.34/–0.24

Computer programs: *APEX3*,[5] *SAINT*,[5] *SADABS*,[5] *SHELXS97*,[6] *SHELXL2014*,[7] *OLEX2*[8]

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Table 1. Crystal data and structure refinement for 4-AcO-DMT fumarate.

Identification code	UMD1651e_a
Empirical formula	$C_{18}H_{22}N_2O_6$
Formula weight	362.37
Temperature/K	296
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	13.0233(11)
b/Å	7.4823(6)
c/Å	19.1016(15)
α/°	90
β/°	103.251(3)
γ/°	90
Volume/Å^3	1811.8(3)
Z	4
ρ_{calc}g/cm^3	1.328
μ/mm^{-1}	0.100
F(000)	768.0
Crystal size/mm^3	0.27 × 0.22 × 0.20
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	5.87 to 50.818
Index ranges	–15 ≤ h ≤ 15, –9 ≤ k ≤ 9, –22 ≤ l ≤ 23
Reflections collected	43099
Independent reflections	3320 [R_{int} = 0.0366, R_{sigma} = 0.0144]
Data/restraints/parameters	3320/0/251
Goodness-of-fit on F^2	1.037
Final R indexes [I ≥ 2σ (I)]	R_1 = 0.0419, wR_2 = 0.1024
Final R indexes [all data]	R_1 = 0.0522, wR_2 = 0.1118
Largest diff. peak/hole / e Å^{-3}	0.34/–0.24

Table 2. Fractional Atomic Coordinates (× 10^4) and Equivalent Isotropic Displacement Parameters (Å^2 × 10^3) for 4-AcO-DMT fumarate. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	768.2(10)	7064.4(16)	4532.0(6)	47.6(3)
O2	1302.9(12)	9574(2)	5142.5(7)	64.6(4)
O3	4888.1(11)	3621.4(17)	3794.7(8)	58.7(4)
O4	6255.3(10)	3995.4(15)	3318.3(7)	50.3(4)
O5	7345.0(13)	–2334.5(19)	3013.4(11)	79.7(5)
O6	5897.2(10)	–2677.1(16)	3410.1(8)	54.7(4)
N1	2709.6(15)	8395(2)	2832.8(10)	56.6(5)
N2	3150.3(12)	3081.5(19)	4305.2(8)	41.6(4)
C1	898(2)	7003(4)	5775.1(12)	75.8(7)
C2	1013.3(14)	8069(3)	5139.2(10)	48.2(4)
C3	815.6(13)	7910(2)	3880.6(9)	38.3(4)
C4	–66.0(15)	8716(3)	3485.2(11)	53.9(5)
C5	–42.6(18)	9510(3)	2829.2(11)	63.2(6)
C6	840.5(19)	9476(2)	2561.4(10)	57.3(5)
C7	1728.8(15)	8615(2)	2962.1(9)	43.0(4)
C8	3330.8(15)	7520(2)	3392.7(12)	52.6(5)
C9	2793.0(13)	7139(2)	3907.2(9)	39.4(4)
C10	1748.3(12)	7828(2)	3637.9(8)	33.7(4)
C11	3268.9(15)	6338(2)	4623.4(11)	51.1(5)
C12	2910.2(16)	4498(2)	4792.1(10)	49.8(5)
C13	2277(2)	2805(3)	3667.5(12)	74.0(7)
C14	3446.2(19)	1379(3)	4698.5(14)	66.4(6)
C15	5584.1(13)	3028(2)	3514.5(9)	36.0(4)
C16	5672.7(13)	1049(2)	3436.0(9)	39.8(4)
C17	6481.1(13)	239(2)	3286.2(9)	41.1(4)
C18	6613.9(13)	–1710(2)	3221.2(9)	39.5(4)

Table 3. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 4-AcO-DMT fumarate. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	57.2(8)	43.9(7)	48.4(7)	–4.4(6)	26.0(6)	–8.6(6)
O2	80.9(10)	59.8(9)	58.3(8)	–15.7(7)	26.3(7)	–22.7(8)
O3	57.7(8)	39.1(7)	92.8(10)	–1.2(7)	45.3(8)	2.6(6)
O4	64.1(8)	23.0(6)	76.8(9)	–1.6(6)	43.1(7)	–3.1(5)
O5	70.7(10)	43.2(8)	144.9(16)	–7.1(9)	65.5(11)	1.7(7)
O6	56.9(8)	22.1(6)	97.5(11)	–2.2(6)	43.5(7)	–1.1(5)
N1	80.0(12)	42.8(9)	60.5(10)	–4.9(8)	44.3(10)	–7.7(8)
N2	45.7(8)	30.9(7)	52.0(9)	–4.3(6)	19.3(7)	–5.5(6)
C1	100.6(18)	81.7(17)	55.1(13)	–0.2(12)	38.7(12)	–14.5(14)
C2	46.9(10)	55.1(12)	48.5(10)	–8.4(9)	23.0(8)	–7.0(9)
C3	41.8(9)	34.5(9)	40.3(9)	–7.3(7)	12.6(7)	–4.3(7)
C4	41.4(10)	53.2(11)	64.7(12)	–14.1(10)	6.9(9)	3.6(8)
C5	67.3(13)	52.4(12)	57.0(12)	–9.5(10)	–12.5(10)	15.4(10)
C6	95.7(16)	35.9(10)	35.2(9)	–3.3(8)	4.2(10)	3.5(10)
C7	65.5(11)	28.3(8)	38.5(9)	–6.9(7)	18.5(8)	–5.4(8)
C8	48.2(10)	40.0(10)	78.0(13)	–14.6(10)	32.1(10)	–5.5(8)
C9	39.0(8)	27.8(8)	52.4(10)	–9.2(7)	12.4(7)	–2.8(7)
C10	41.1(8)	25.0(7)	36.2(8)	–6.7(6)	11.3(6)	–4.5(6)
C11	50.3(10)	35.6(9)	59.7(11)	–12.0(8)	–3.2(8)	6.2(8)
C12	67.5(12)	41.6(10)	40.5(9)	–2.7(8)	12.7(8)	10.3(9)
C13	82.2(16)	69.9(15)	63.6(13)	–20.4(12)	3.5(12)	–16.9(13)
C14	80.3(15)	33.3(10)	92.8(16)	7.8(10)	34.5(13)	2.3(10)
C15	40.7(8)	26.8(8)	43.3(9)	1.9(7)	15.2(7)	0.5(7)
C16	42.0(9)	25.1(8)	55.6(10)	0.9(7)	17.9(8)	–6.3(7)
C17	43.3(9)	26.9(8)	56.8(10)	1.0(7)	19.2(8)	–6.2(7)
C18	38.0(9)	30.7(8)	53.0(10)	0.2(7)	17.1(7)	1.2(7)

Table 4. Bond Lengths for 4-AcO-DMT fumarate.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C2	1.357(2)	C3	C4	1.362(3)
O1	C3	1.410(2)	C3	C10	1.397(2)
O2	C2	1.187(2)	C4	C5	1.394(3)
O3	C15	1.2360(19)	C5	C6	1.362(3)
O4	C15	1.2565(19)	C6	C7	1.391(3)
O5	C18	1.207(2)	C7	C10	1.414(2)
O6	C18	1.296(2)	C8	C9	1.361(3)
N1	C7	1.365(2)	C9	C10	1.435(2)
N1	C8	1.353(3)	C9	C11	1.492(3)
N2	C12	1.490(2)	C11	C12	1.512(3)
N2	C13	1.478(3)	C15	C16	1.495(2)
N2	C14	1.484(2)	C16	C17	1.302(2)
C1	C2	1.490(3)	C17	C18	1.477(2)

Table 5. Bond Angles for 4-AcO-DMT fumarate.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C2	O1	C3	117.16(13)	N1	C8	C9	111.00(17)
C8	N1	C7	109.27(16)	C8	C9	C10	105.57(16)
C13	N2	C12	112.46(16)	C8	C9	C11	124.86(17)
C13	N2	C14	111.02(17)	C10	C9	C11	129.29(15)
C14	N2	C12	111.21(15)	C3	C10	C7	116.73(15)
O1	C2	C1	110.61(17)	C3	C10	C9	136.17(15)
O2	C2	O1	122.83(17)	C7	C10	C9	107.10(14)
O2	C2	C1	126.53(19)	C9	C11	C12	118.53(15)
C4	C3	O1	119.10(16)	N2	C12	C11	113.29(15)
C4	C3	C10	121.46(16)	O3	C15	O4	123.46(15)
C10	C3	O1	119.38(15)	O3	C15	C16	118.71(14)
C3	C4	C5	119.87(19)	O4	C15	C16	117.75(14)
C6	C5	C4	121.62(18)	C17	C16	C15	124.60(15)
C5	C6	C7	118.01(18)	C16	C17	C18	126.45(15)
N1	C7	C6	130.62(18)	O5	C18	O6	123.26(16)
N1	C7	C10	107.06(16)	O5	C18	C17	121.76(16)
C6	C7	C10	122.28(17)	O6	C18	C17	114.97(14)

Table 6. Hydrogen Bonds for 4-AcO-DMT fumarate**.**

D	H	A	d(D–H)/Å	d(H–A)/Å	d(D–A)/Å	D–H–A/°
N1	H1	O4[1]	0.86(3)	2.03(3)	2.866(2)	165(3)
O6	H6A	O4[2]	0.99(3)	1.56(3)	2.5465(16)	178(3)
N2	H2	O3	0.90(2)	1.80(2)	2.6922(19)	168(2)

[1]1–X,1/2+Y,1/2–Z; [2]+X,–1+Y,+Z

Table 7. Torsion Angles for 4-AcO-DMT fumarate.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O1	C3	C4	C5	–178.04(16)	C6	C7	C10	C3	1.8(2)
O1	C3	C10	C7	176.57(13)	C6	C7	C10	C9	–177.53(15)
O1	C3	C10	C9	–4.4(3)	C7	N1	C8	C9	–0.2(2)
O3	C15	C16	C17	–165.73(18)	C8	N1	C7	C6	177.58(18)
O4	C15	C16	C17	11.3(3)	C8	N1	C7	C10	–0.11(19)
N1	C7	C10	C3	179.69(14)	C8	C9	C10	C3	–179.62(18)
N1	C7	C10	C9	0.40(17)	C8	C9	C10	C7	–0.54(17)
N1	C8	C9	C10	0.5(2)	C8	C9	C11	C12	–115.2(2)
N1	C8	C9	C11	–173.97(16)	C9	C11	C12	N2	62.5(2)
C2	O1	C3	C4	–90.7(2)	C10	C3	C4	C5	–1.2(3)
C2	O1	C3	C10	92.34(18)	C10	C9	C11	C12	71.8(2)
C3	O1	C2	O2	–3.3(3)	C11	C9	C10	C3	–5.5(3)
C3	O1	C2	C1	178.44(16)	C11	C9	C10	C7	173.59(16)
C3	C4	C5	C6	1.3(3)	C13	N2	C12	C11	–91.2(2)
C4	C3	C10	C7	–0.3(2)	C14	N2	C12	C11	143.59(17)
C4	C3	C10	C9	178.74(17)	C15	C16	C17	C18	178.39(17)
C4	C5	C6	C7	0.2(3)	C16	C17	C18	O5	172.8(2)
C5	C6	C7	N1	–179.10(18)	C16	C17	C18	O6	–7.9(3)
C5	C6	C7	C10	–1.7(3)					

Table 8. Hydrogen Atom Coordinates (Å × 10^4) and Isotropic Displacement Parameters (Å^2 × 10^3) for 4-AcO-DMT fumarate.

Atom	*x*	*y*	*z*	U(eq)
H6A	6040(20)	–3960(40)	3366(14)	90(8)
H1	2950(20)	8740(40)	2473(15)	93(9)
H2	3707(17)	3420(30)	4128(11)	58(6)
H1A	732	7785	6132	114
H1B	1546	6389	5973	114
H1C	340	6147	5630	114
H4	–683	8736	3653	65
H5	–645	10078	2568	76
H6	849	10013	2124	69
H8	4032	7218	3422	63
H11A	3139	7151	4989	61
H11B	4027	6292	4673	61
H12A	3251	4196	5284	60
H12B	2155	4524	4756	60
H13A	2512	2049	3329	111
H13B	2058	3938	3447	111
H13C	1694	2250	3812	111
H14A	3619	504	4377	100
H14B	2865	958	4884	100
H14C	4046	1575	5089	100
H16	5111	348	3498	48
H17	7029	959	3213	49