Supporting Information:

Receptor binding profiles for tryptamine psychedelics and effects of 4-propionoxy-*N,N*-dimethyltryptamine in mice

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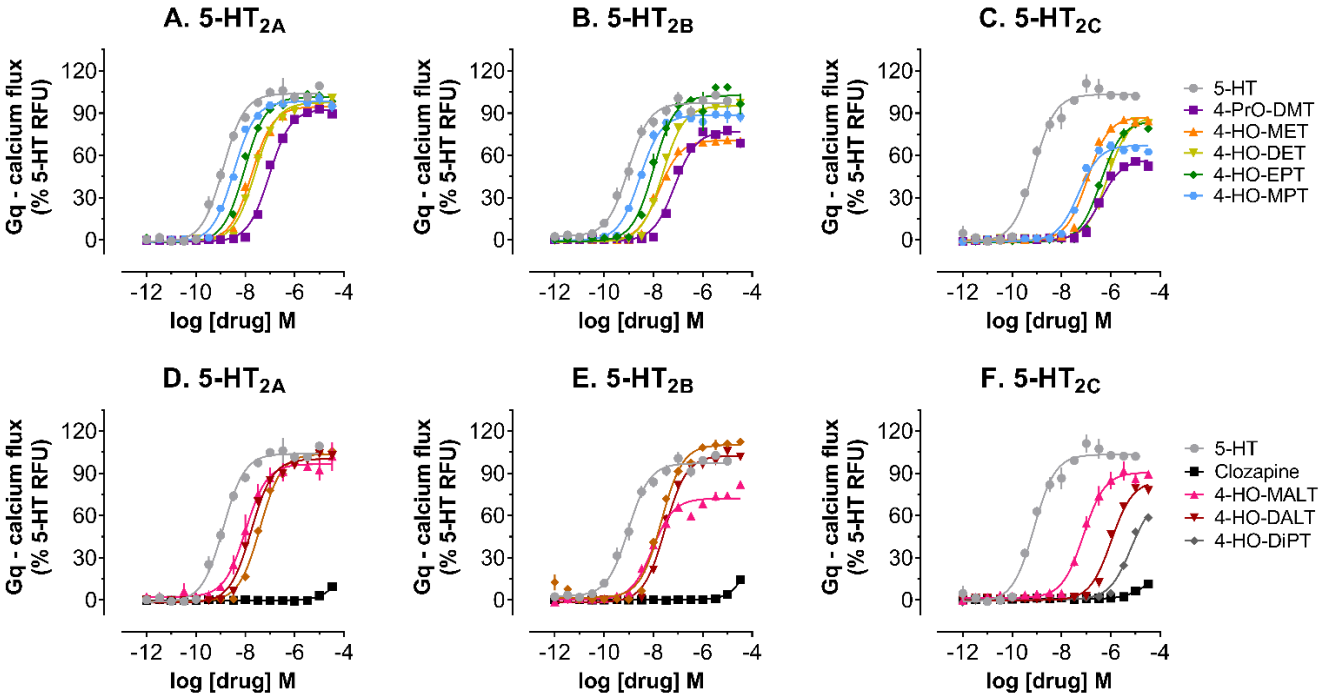


Figure S1. Concentration-response curves for agonist activity of 4-PrO-DMT and several other tryptamine psychedelics for G_q-calcium mobilization at human 5-HT_2 receptors. All values are relative to 5-HT (% 5-HT relative fluorescence unit or RFU) and are mean ± SEM. Potency and efficacy values are shown in **Table S1**.

Compound	5-HT$_{2A}$ G_q-Calcium Mobilization			5-HT$_{2B}$ G_q-Calcium Mobilization			5-HT$_{2C}$ G_q-Calcium Mobilization		
	EC_{50} (nM)	95% CI	E_{max} (% 5-HT)	EC_{50} (nM)	95% CI	E_{max} (%)	EC_{50} (nM)	95% CI (nM)	E_{max} (%)
4-PrO-DMT	93.4	81.8 - 106.7	92.8	71.5	58.7 - 87.1	76.9	390.3	320.8 - 474.9	56.9
4-HO-MET	18.3	15.9 - 21.1	94.6	16.7	14.4 - 19.4	70.7	112.9	95.8 - 133.0	87.2
4-HO-DET	25.4	22.4 - 28.7	97.5	23.8	20.7 - 27.2	95.1	729.3	623.5 - 853.1	87.7
4-HO-EPT	9.3	7.9 - 10.9	101.4	10.3	7.6 - 13.9	102.4	393.3	331.5 - 466.7	84.4
4-HO-MPT	3.4	2.9 - 3.9	98.4	2.8	2.3 - 3.4	88.7	49.8	40.1 - 61.9	67.2
4-HO-MALT	10.2	7.0 - 15.0	96.5	9.1	7.1 - 11.7	72.1	77.7	59.6 - 101.4	90.6
4-HO-DALT	17.4	15.0 - 20.0	100.2	29.6	25.8 - 33.9	102.4	1,051	888.0 – 1,244	84.5
4-HO-DiPT	39.8	35.4 - 44.7	103.7	20.9	17.1 - 25.6	110.2	6,442	5,335 – 7,777	72.4
Clozapine	> 10,000	x	x	>10,000	x	x	>10,000	x	x

Table S1. Agonist potency (EC_{50} & 95% CI) and efficacy (E_{max}) of 4-PrO-DMT and several other tryptamine psychedelics for G_q-calcium mobilization at human 5-HT$_2$ receptors relative to 5-HT. Concentration-response curves are depicted in **Figure S1** and details for the assays can be found online at https://pdsp.unc.edu/pdspweb/content/UNC-CH%20Protocol%20Book.pdf . All values are normalized to % 5-HT response. 5-HT displayed EC_{50} values = 1.3, 0.9, and 0.8 nM for 5-HT$_{2A}$, 5-HT$_{2B}$, and 5-HT$_{2C}$ respectively. Data represent 1 – 2 experiments with triplicate determinations.

Drug	Dose (mg/kg)	HTR count (mean ± SEM)	Post Test *p* value	Temperature Change (mean ± SEM)	Post Test *p* value	Locomotor Activity (mean ± SEM)	Post Test *p* value
4-PrO-DMT	0	7.2 ± 1.1	-	-0.5 ± 0.1	-	2,953 ± 206	-
	0.03	5.2 ± 0.6	0.9507	-0.5 ± 0.1	0.9999	2,432 ± 216	0.4451
	0.1	9.2 ± 0.2	0.9576	-0.5 ± 0.2	> 0.9999	2,837 ± 243	0.9995
	0.3	**15.5 ± 1.7**	**0.0132**	-0.7 ± 0.2	0.9979	3,018 ± 315	0.9997
	1	**30.4 ± 2.1**	**< 0.0001**	-0.9 ± 0.1	0.9250	2,927 ± 270	> 0.9999
	3	**23.2 ± 3.7**	**< 0.0001**	**-2.2 ± 0.3**	**0.0089**	**1,911 ± 301**	**0.0219**
	10	9.0 ± 2.5	0.9748	**-3.8 ± 0.6**	**< 0.0001**	**1,032 ± 211**	**< 0.0001**
	30	5.5 ± 1.4	0.9804	**-7.3 ± 0.7**	**< 0.0001**	**404 ± 67**	**< 0.0001**

Table S2. Mean ± SEM (n = 5 – 6) and post hoc test comparisons for dose-response effects of 4-PrO-DMT to produce HTR (count/30 min), hypothermia (°C), and hypolocomotion (distance traveled cm) in mice. Extension of **Figures 2 and 3**. Bold values are statistically significant values vs. vehicle control (0 mg/kg) and other relevant statistical information can be found in the **Materials and Methods** section. Overall F-test values were $F_{7,36}$ = 23.28 p < 0.0001, $F_{7,36}$ = 46.52 p < 0.0001, and $F_{7,36}$ = 18.02 p < 0.0001 for HTR, temperature change, and locomotor activity comparisons respectively.

Drug	Dose M100907 / Drug (mg/kg)	HTR count (mean ± SEM)	Temperature Change (mean ± SEM)	Locomotor Activity (mean ± SEM)
4-PrO-DMT	0 / 0	5.0 ± 2.0	-0.6 ± 0.2	4,075 ± 538
	0.01 / 0	1.0 ± 0.5	-0.02 ± 0.1	3,140 ± 302
	0 / 0.6	18 ± 1.2	-0.3 ± 0.2	3,941 ± 510
	0.01 / 0.6	1.0 ± 0.4	-0.1 ± 0.1	3,108 ± 485

Table S3. Mean ± SEM (*n* = 5 – 6) for 5-HT_{2A} antagonist pretreatment effects of M100907 on HTR (count/30 min), temperature change (°C), and locomotor activity (distance traveled cm) induced by 4-PrO-DMT. Extension of **Figure 4A** and **Figure S2A – B**.

Groups Compared	HTR		Temperature Change		Locomotor Activity	
Tukey's Test	**Summary**	***p* value**	**Summary**	***p* value**	**Summary**	***p* value**
0 / 0 vs. 0.01 / 0	ns	0.1390	ns	0.0783	ns	0.5611
0 / 0 vs. 0.01 / 0.6	ns	0.1159	ns	0.4052	ns	0.9972
0 / 0 vs. 0 / 0.6	*	**< 0.0001**	ns	0.0814	ns	0.4987
0.01 / 0 vs. 0.01 / 0.6	ns	> 0.9999	ns	0.6855	ns	0.6439
0.01 / 0 vs. 0 / 0.6	*	**< 0.0001**	ns	0.9991	ns	> 0.9999
0.01 / 0.6 vs. 0 / 0.6	*	**< 0.0001**	ns	0.7363	ns	0.5796

Table S4. Post hoc test comparisons for M100907 pretreatment on effects of 4-PrO-DMT. Extension of **Figure 4A** and **Figure S2A – B**. Bold values are statistically significant values. Overall *F*-test values were $F_{3,18} = 49.45$ $p < 0.0001$, $F_{3,18} = 2.95$ $p = 0.0604$, and $F_{3,18} = 1.15$ $p = 0.3562$ for HTR, temperature change, and locomotor activity comparisons respectively.

Drug	Dose WAY100635 / Drug (mg/kg)	HTR count (mean ± SEM)	Temperature Change (mean ± SEM)	Locomotor Activity (mean ± SEM)
4-PrO-DMT	0 / 0	3.0 ± 1.2	-0.3 ± 0.1	1,760 ± 351
	3 / 0	3.0 ± 0.5	-0.2 ± 0.1	1,607 ± 371
	0 / 10	8.2 ± 3.1	-4.1 ± 0.7	687 ± 163
	3 / 10	25.2 ± 2.7	-2.0 ± 0.3	1,331 ± 267

Table S5. Mean ± SEM (*n* = 5 – 6) for 5-HT_{1A} antagonist pretreatment effects of WAY100635 on HTR (count/30 min), temperature change (°C), and locomotor activity (distance traveled cm) induced by 4-PrO-DMT. Extension of **Figure 4B – C** and **Figure S2D.**

Groups Compared	HTR		Temperature Change		Locomotor Activity	
Tukey's Test	**Summary**	***p* value**	**Summary**	***p* value**	**Summary**	***p* value**
0 / 0 vs. 3 / 0	ns	> 0.9999	ns	0.9996	ns	0.9837
0 / 0 vs. 0 / 10	ns	0.4411	*	**< 0.0001**	ns	0.0733
0 / 0 vs. 3 / 10	*	**< 0.0001**	*	**0.0345**	ns	0.7222
3 / 0 vs. 0 / 10	ns	0.4411	*	**< 0.0001**	ns	0.1461
3 / 0 vs. 3 / 10	*	**< 0.0001**	*	**0.0280**	ns	0.9045
0 / 10 vs. 3 / 10	*	**0.0003**	*	**0.0074**	ns	0.3745

Table S6. Post hoc test comparisons for WAY100635 pretreatment on effects of 4-PrO-DMT. Extension of **Figure 4B – C** and **Figure S2D**. Bold values are statistically significant values. Overall *F*-test values were $F_{3,18} = 20.22$ $p < 0.0001$, $F_{3,18} = 20.33$ $p < 0.0001$, and $F_{3,18} = 2.78$ $p = 0.0709$ for HTR, temperature change, and locomotor activity comparisons respectively

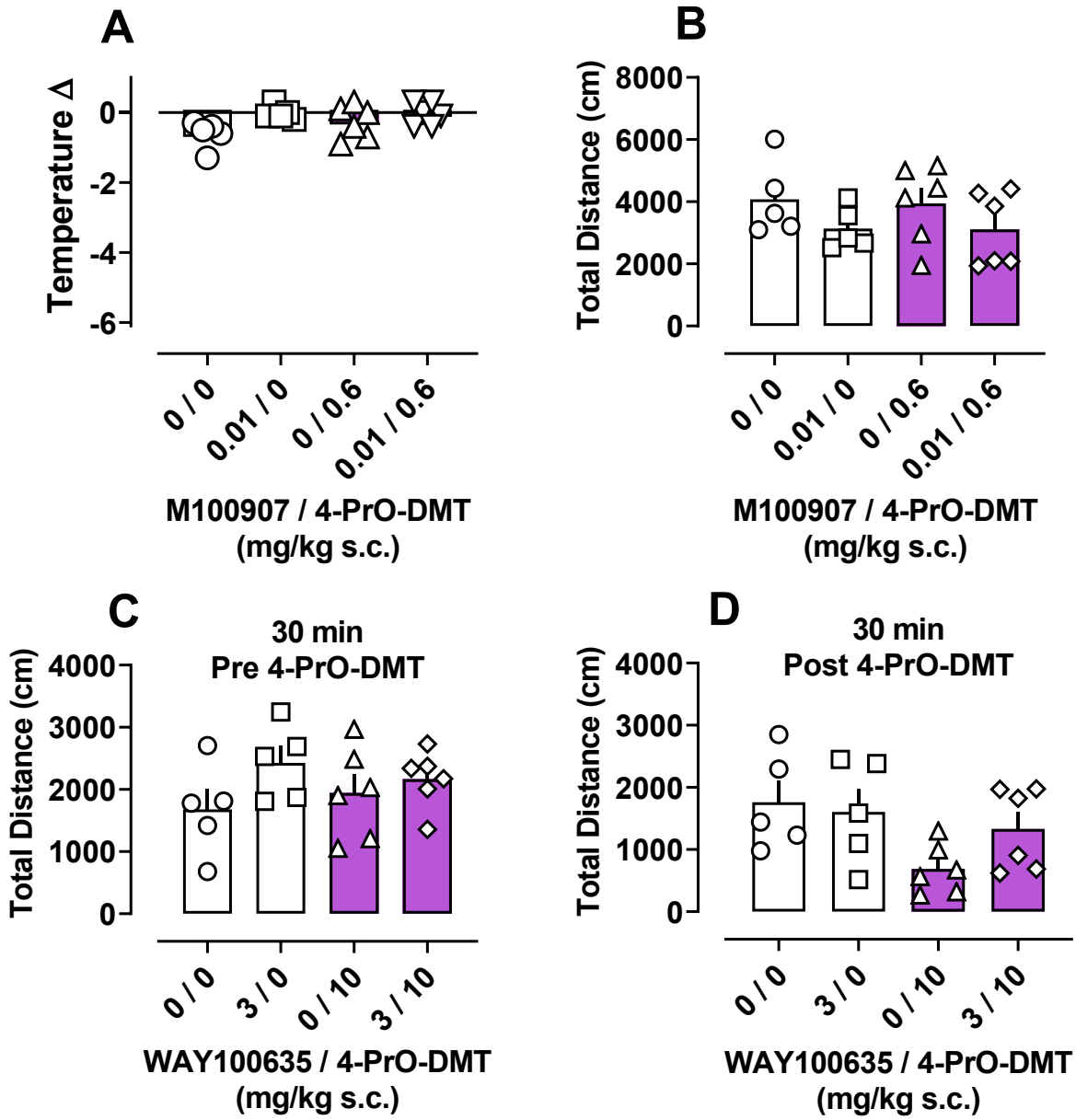
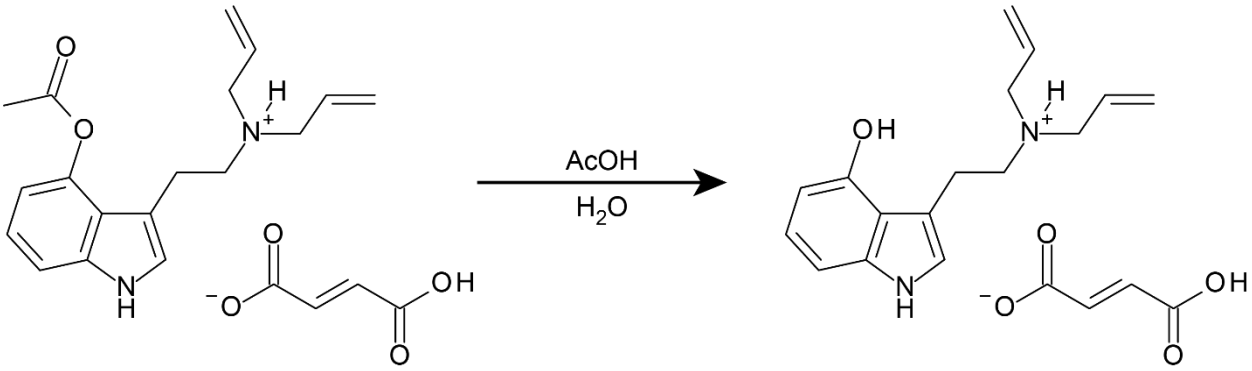


Figure S2. Effects of M100907 or WAY100635 pretreatment on body temperature (°C) and locomotor activity (distance traveled cm). (A) Temperature change for the 30 min session after 4-PrO-DMT administration. (B) Distance traveled over the full 60-minute session from M100907 administration through the end of the session (30 min after 4-PrO-DMT). (C) Effects of WAY100635 or vehicle pretreatment on locomotor activity. (D) Effects of vehicle or 4-PrO-DMT treatment on locomotor activity in WAY100635 or vehicle treated mice.

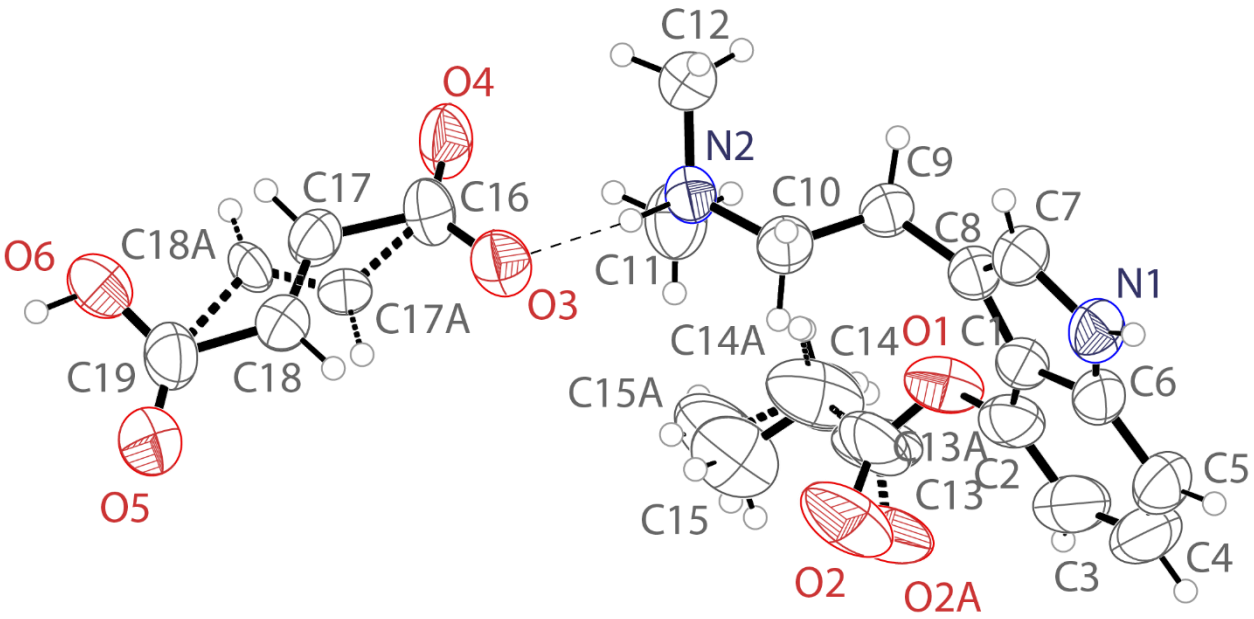


Synthesis and crystallization of 4-HO-DALT hydrofumarate

150 mg (1mmol) of 4-acetoxy-*N*,*N*-diallyltryptammonium hydrofumarate was dissolved in 1.0 mL of water, and an excess of acetic acid (6.0 mL) was added. The mixture was refluxed overnight under an atmosphere of nitrogen. Solvent was removed in vacuo, and acetone was added and filtered. Solvent was removed *in vacuo* from the filtrate to obtain yellow oil. The oil was triturated with pentane to produce a solid which was recrystallized in acetone/pentane mixture to yield a crystalline product.

^{1}H NMR (400 MHz, D_2O): δ 7.19 (s, 1H, Ar*H*), 7.08 (m, 1H, Ar*H*), 6.63 (s, 1H, C*H*), 6.55 (dd, *J* = 6.1, 2.3 Hz, 1H, Ar*H*), 5.98 – 5.74 (m, 2H, C*H*), 5.61-5.54 (m, 4H, CH_2), 3.82 (d, *J* = 7.1 Hz, 4H, CH_2), 3.55 (t, *J* = 7.4 Hz, 2H, CH_2), 3.30 (t, *J* = 7.5 Hz, 2H, CH_2).

Figure S3. Fully labelled displacement ellipsoid representation (50%) of 4-PrO-DMT hydrofumarate



X-Ray data collection and refinement details for 4-PrO-DMT hydrofumarate. Crystals suitable for X-ray diffraction studies were grown from the slow evaporation of an aqueous solution. All operations were performed on a Bruker D8 Venture CMOS diffractometer, using MoKα radiation with a TRIUMPH monochromator. Data collection was carried out using the Bruker *APEX3* software. Cell refinement and data reduction were performed with the *SAINT* program.[1] The structure solution was done with the *SHELXT2014*[2] and structure refinement was performed with *SHELXL2018*.[3] Further refinement and molecular graphics were generated using the *OLEX2* software.[4]

The asymmetric unit contained one protonated tryptammonium cation and one singly protonated hydrofumarate anion. All non-hydrogen atoms were refined anisotropically (XL) by full matrix least squares on F^2. H1, H2 and H6 were found from a Fourier difference map. H1 and H2 refined freely with isotropic displacement parameters of 1.20 times U_{eq} of the parent N atoms. H6 was refined with a fixed distance of 0.90 (0.01) Å and an isotropic displacement parameter of 1.50 times U_{eq} of the parent O atom. All other hydrogen atoms were placed in calculated positions with a riding model with C–H lengths of 0.93 Å (sp^2), 0.96 Å (CH_3), and 0.97 Å (CH_2) with isotropic displacement parameters set to 1.20 (sp^2 and CH_2), and 1.50 (CH_3) times U_{eq} of the parent C atom. The propionoxy group (O2, C13, C14, C15) are modeled as a two-component disorder with a 0.51(3) to 0.49(3) occupancy ratio. C17 and C18 of the hydrofumarate anion are also modeled as a two-component disorder with a 0.826(8) to 0.174(8) occupancy ratio. Further details are in the tables below, and final CIF is available as supporting material.

Table S7. Crystal data, data collection and refinement for 4-PrO-DMT hydrofumarate

$C_{15}H_{21}N_2O_2 \cdot C_4H_3O_4$	$F(000) = 800$
$M_r = 376.40$	$D_x = 1.274$ Mg m^{-3}
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Hall symbol: -P 2yn	Cell parameters from 9336 reflections
$a = 11.7169$ (19) Å	$\Theta = 2.6–24.7°$
$b = 11.4642$ (16) Å	$\mu = 0.10$ mm^{-1}
$c = 15.287$ (2) Å	$T = 297$ K
$\beta = 107.076$ (5)°	Block, colourless
$V = 1963.0$ (5) Å^3	0.28 × 0.22 × 0.18 mm
$Z = 4$	
Bruker D8 Venture CMOS diffractometer	2649 reflections with $I > 2\sigma(I)$
Radiation source: Mo Kα	$R_{int} = 0.041$
φ and ω scans	$\Theta_{max} = 25.4°$, $\Theta_{min} = 2.6°$
Absorption correction: multi-scan *SADABS2016*/2 (Bruker,2016/2)	$h = -14 \rightarrow 14$
$T_{min} = 0.701$, $T_{max} = 0.745$	$k = -13 \rightarrow 13$
37620 measured reflections	$l = -18 \rightarrow 18$
3543 independent reflections	
Refinement on F^2	74 restraints
Least-squares matrix: full	Hydrogen site location: mixed
$R[F^2 > 2\sigma(F^2)] = 0.050$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.147$	$w = 1/[\sigma^2(F_o^2) + (0.0695P)^2 + 0.5927P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.03$	$(\Delta/\sigma)_{max} = 0.001$
3543 reflections	$\Delta\rho_{max} = 0.22$ e Å^{-3}
316 parameters	$\Delta\rho_{min} = -0.22$ e Å^{-3}

Table S8. Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2) for 4-PrO-DMT hydrofumarate

	x	*y*	*z*	U_{iso}*/U_{eq}	Occ. (<1)
O1	0.40448 (14)	0.57590 (16)	0.32665 (11)	0.0810 (5)	
N1	0.1589 (2)	0.83715 (15)	0.41522 (13)	0.0705 (5)	
H1	0.129 (2)	0.895 (2)	0.4345 (18)	0.086 (8)*	
N2	0.14531 (15)	0.32863 (14)	0.41927 (12)	0.0586 (4)	
H2	0.158 (2)	0.295 (2)	0.4791 (18)	0.083 (7)*	
C1	0.28354 (17)	0.71444 (17)	0.37490 (12)	0.0568 (5)	
C2	0.39301 (19)	0.6874 (2)	0.36085 (14)	0.0692 (6)	
C3	0.4812 (2)	0.7703 (3)	0.37387 (17)	0.0906 (8)	
H3	0.553898	0.751172	0.364522	0.109*	
C4	0.4624 (3)	0.8824 (3)	0.40086 (19)	0.1006 (10)	
H4	0.523129	0.937300	0.409170	0.121*	
C5	0.3580 (3)	0.9142 (2)	0.41550 (17)	0.0880 (8)	
H5	0.346121	0.989897	0.432877	0.106*	
C6	0.2690 (2)	0.82949 (17)	0.40362 (13)	0.0655 (6)	
C7	0.10251 (19)	0.73193 (17)	0.39438 (14)	0.0643 (5)	
H7	0.025895	0.715878	0.397265	0.077*	
C8	0.17447 (17)	0.65386 (16)	0.36875 (12)	0.0551 (5)	
C9	0.14375 (18)	0.52806 (16)	0.34490 (13)	0.0564 (5)	
H9A	0.193137	0.497877	0.309063	0.068*	
H9B	0.060829	0.521695	0.308578	0.068*	
C10	0.1645 (2)	0.45781 (16)	0.43202 (13)	0.0632 (5)	
H10A	0.245827	0.471098	0.469742	0.076*	
H10B	0.111702	0.487132	0.465363	0.076*	

C11	0.2316 (2)	0.2727 (2)	0.37879 (19)	0.0841 (7)	
H11A	0.311441	0.290825	0.415186	0.126*	
H11B	0.219263	0.301247	0.317671	0.126*	
H11C	0.220265	0.189715	0.377223	0.126*	
C12	0.0209 (2)	0.2982 (2)	0.36825 (18)	0.0798 (7)	
H12A	-0.032912	0.336506	0.395690	0.120*	
H12B	0.010338	0.215258	0.370147	0.120*	
H12C	0.004435	0.322970	0.305790	0.120*	
O2	0.5514 (16)	0.5240 (16)	0.4480 (5)	0.122 (5)	0.51 (3)
C13	0.4947 (10)	0.5094 (10)	0.3682 (6)	0.093 (4)	0.51 (3)
C14	0.5003 (12)	0.4030 (11)	0.3144 (7)	0.087 (4)	0.51 (3)
H14A	0.524775	0.423417	0.261012	0.104*	0.51 (3)
H14B	0.422037	0.366943	0.293741	0.104*	0.51 (3)
C15	0.589 (2)	0.3189 (18)	0.3737 (12)	0.110 (4)	0.51 (3)
H15A	0.582598	0.244987	0.343168	0.165*	0.51 (3)
H15B	0.571478	0.309034	0.430902	0.165*	0.51 (3)
H15C	0.667962	0.349186	0.384704	0.165*	0.51 (3)
O2A	0.5875 (11)	0.5544 (10)	0.4158 (18)	0.144 (5)	0.49 (3)
C13A	0.4988 (7)	0.5095 (11)	0.3644 (8)	0.092 (4)	0.49 (3)
C14A	0.4959 (13)	0.3945 (12)	0.3186 (10)	0.111 (5)	0.49 (3)
H14C	0.514299	0.409356	0.261694	0.134*	0.49 (3)
H14D	0.413764	0.367888	0.301955	0.134*	0.49 (3)
C15A	0.572 (2)	0.293 (2)	0.3633 (16)	0.147 (8)	0.49 (3)
H15D	0.564938	0.231686	0.319431	0.220*	0.49 (3)
H15E	0.545630	0.265547	0.413425	0.220*	0.49 (3)
H15F	0.653711	0.317620	0.385591	0.220*	0.49 (3)
O3	0.19066 (14)	0.20109 (13)	0.57933 (9)	0.0733 (4)	
O4	0.12423 (17)	0.05871 (12)	0.48175 (11)	0.0851 (5)	
O5	0.35860 (18)	-0.04667 (16)	0.86211 (13)	0.0957 (6)	
O6	0.23761 (17)	-0.17353 (17)	0.77237 (11)	0.0926 (6)	
H6	0.260 (3)	-0.219 (2)	0.8218 (15)	0.127 (11)*	

C16	0.16768 (19)	0.09418 (17)	0.55962 (14)	0.0611 (5)	
C19	0.2894 (2)	-0.0703 (2)	0.79104 (17)	0.0706 (6)	
C17	0.1922 (3)	0.0009 (3)	0.6339 (2)	0.0592 (9)	0.826 (8)
H17	0.158958	-0.072678	0.618462	0.071*	0.826 (8)
C18	0.2564 (2)	0.0188 (3)	0.7167 (2)	0.0619 (9)	0.826 (8)
H18	0.284822	0.094145	0.731726	0.074*	0.826 (8)
C17A	0.2348 (12)	0.0563 (12)	0.6596 (11)	0.057 (4)	0.174 (8)
H17A	0.278819	0.108896	0.702749	0.068*	0.174 (8)
C18A	0.2257 (11)	-0.0517 (11)	0.6787 (9)	0.058 (4)	0.174 (8)
H18A	0.189790	-0.109632	0.637187	0.070*	0.174 (8)

Table S9. Atomic displacement parameters (Å^2) for 4-PrO-DMT hydrofumarate

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0650 (10)	0.1046 (13)	0.0646 (9)	0.0033 (8)	0.0054 (7)	-0.0184 (9)
N1	0.0909 (14)	0.0454 (10)	0.0686 (11)	0.0010 (9)	0.0132 (10)	-0.0056 (8)
N2	0.0654 (10)	0.0498 (9)	0.0557 (9)	0.0009 (7)	0.0104 (8)	0.0064 (7)
C1	0.0659 (12)	0.0569 (11)	0.0409 (9)	-0.0100 (9)	0.0054 (8)	0.0013 (8)
C2	0.0675 (13)	0.0868 (15)	0.0465 (10)	-0.0127 (11)	0.0061 (9)	-0.0044 (10)
C3	0.0742 (15)	0.127 (2)	0.0662 (14)	-0.0320 (15)	0.0143 (12)	-0.0030 (15)
C4	0.103 (2)	0.109 (2)	0.0778 (17)	-0.0554 (18)	0.0078 (15)	-0.0009 (16)
C5	0.116 (2)	0.0656 (14)	0.0684 (14)	-0.0315 (14)	0.0044 (14)	0.0016 (11)
C6	0.0832 (15)	0.0525 (11)	0.0506 (11)	-0.0138 (10)	0.0039 (10)	0.0014 (8)
C7	0.0719 (13)	0.0502 (11)	0.0676 (12)	-0.0022 (9)	0.0153 (10)	-0.0031 (9)
C8	0.0644 (11)	0.0470 (10)	0.0484 (10)	-0.0037 (8)	0.0082 (8)	-0.0004 (8)
C9	0.0649 (11)	0.0489 (10)	0.0508 (10)	-0.0055 (8)	0.0095 (8)	-0.0040 (8)

C10	0.0802 (13)	0.0528 (11)	0.0506 (10)	-0.0071 (9)	0.0097 (9)	-0.0037 (9)
C11	0.0933 (17)	0.0659 (14)	0.0995 (18)	0.0157 (12)	0.0385 (14)	0.0080 (13)
C12	0.0716 (14)	0.0616 (13)	0.0915 (16)	-0.0097 (11)	0.0010 (12)	0.0118 (11)
O2	0.130 (7)	0.148 (8)	0.062 (4)	0.040 (5)	-0.011 (3)	-0.019 (3)
C13	0.105 (9)	0.107 (7)	0.046 (5)	0.009 (6)	-0.010 (5)	0.005 (5)
C14	0.082 (7)	0.137 (9)	0.051 (5)	-0.008 (6)	0.034 (5)	-0.002 (4)
C15	0.123 (8)	0.115 (7)	0.089 (6)	0.032 (5)	0.025 (6)	-0.027 (5)
O2A	0.087 (5)	0.154 (5)	0.142 (11)	-0.003 (4)	-0.043 (5)	0.007 (6)
C13A	0.035 (5)	0.140 (9)	0.097 (9)	0.011 (5)	0.014 (4)	-0.020 (7)
C14A	0.069 (8)	0.138 (9)	0.117 (10)	0.043 (7)	0.011 (6)	-0.038 (7)
C15A	0.136 (11)	0.143 (12)	0.125 (11)	0.056 (11)	-0.018 (8)	-0.002 (9)
O3	0.1015 (11)	0.0614 (9)	0.0510 (8)	0.0062 (8)	0.0131 (7)	-0.0061 (6)
O4	0.1360 (15)	0.0464 (8)	0.0652 (10)	-0.0005 (8)	0.0176 (9)	0.0013 (7)
O5	0.1027 (13)	0.0877 (12)	0.0841 (12)	-0.0121 (10)	0.0078 (10)	0.0171 (10)
O6	0.1065 (13)	0.1025 (14)	0.0533 (9)	-0.0144 (11)	-0.0007 (9)	0.0144 (9)
C16	0.0771 (13)	0.0510 (11)	0.0580 (12)	0.0140 (9)	0.0240 (10)	0.0072 (9)
C19	0.0728 (14)	0.0689 (14)	0.0734 (15)	0.0034 (11)	0.0267 (12)	0.0212 (12)
C17	0.0718 (19)	0.0467 (16)	0.0567 (19)	-0.0087 (15)	0.0148 (14)	-0.0021 (16)
C18	0.0669 (16)	0.0538 (17)	0.060 (2)	-0.0065 (13)	0.0099 (13)	0.0028 (16)
C17A	0.062 (8)	0.050 (8)	0.045 (8)	-0.012 (6)	-0.003 (6)	-0.004 (6)
C18A	0.076 (8)	0.047 (8)	0.034 (6)	-0.004 (6)	-0.011 (5)	0.011 (6)

Table S10. Geometric parameters (Å, º) for 4-PrO-DMT hydrofumarate

O1—C2	1.402 (3)	C12—H12C	0.9600
O1—C13	1.307 (8)	O2—C13	1.217 (10)
O1—C13A	1.327 (8)	C13—C14	1.484 (10)
N1—H1	0.84 (3)	C14—H14A	0.9700

N1—C6	1.355 (3)	C14—H14B	0.9700
N1—C7	1.367 (3)	C14—C15	1.507 (11)
N2—H2	0.96 (3)	C15—H15A	0.9600
N2—C10	1.502 (2)	C15—H15B	0.9600
N2—C11	1.478 (3)	C15—H15C	0.9600
N2—C12	1.479 (3)	O2A—C13A	1.218 (11)
C1—C2	1.396 (3)	C13A—C14A	1.488 (11)
C1—C6	1.416 (3)	C14A—H14C	0.9700
C1—C8	1.433 (3)	C14A—H14D	0.9700
C2—C3	1.375 (3)	C14A—C15A	1.500 (11)
C3—H3	0.9300	C15A—H15D	0.9600
C3—C4	1.386 (4)	C15A—H15E	0.9600
C4—H4	0.9300	C15A—H15F	0.9600
C4—C5	1.357 (4)	O3—C16	1.272 (2)
C5—H5	0.9300	O4—C16	1.219 (2)
C5—C6	1.398 (3)	O5—C19	1.181 (3)
C7—H7	0.9300	O6—H6	0.894 (10)
C7—C8	1.364 (3)	O6—C19	1.322 (3)
C8—C9	1.505 (3)	C16—C17	1.524 (4)
C9—H9A	0.9700	C16—C17A	1.561 (15)
C9—H9B	0.9700	C19—C18	1.492 (4)
C9—C10	1.514 (3)	C19—C18A	1.673 (13)
C10—H10A	0.9700	C17—H17	0.9300
C10—H10B	0.9700	C17—C18	1.286 (5)
C11—H11A	0.9600	C18—H18	0.9300
C11—H11B	0.9600	C17A—H17A	0.9300
C11—H11C	0.9600	C17A—C18A	1.283 (18)
C12—H12A	0.9600	C18A—H18A	0.9300
C12—H12B	0.9600		
C13—O1—C2	120.2 (5)	H12A—C12—H12B	109.5
C13A—O1—C2	121.3 (5)	H12A—C12—H12C	109.5
C6—N1—H1	127.2 (18)	H12B—C12—H12C	109.5
C6—N1—C7	109.00 (19)	O1—C13—C14	111.8 (8)
C7—N1—H1	123.7 (18)	O2—C13—O1	122.2 (9)

C10—N2—H2	107.2 (14)	O2—C13—C14	124.7 (10)
C11—N2—H2	106.7 (14)	C13—C14—H14A	109.9
C11—N2—C10	112.78 (17)	C13—C14—H14B	109.9
C11—N2—C12	111.50 (19)	C13—C14—C15	109.1 (11)
C12—N2—H2	105.3 (14)	H14A—C14—H14B	108.3
C12—N2—C10	112.83 (16)	C15—C14—H14A	109.9
C2—C1—C6	117.03 (19)	C15—C14—H14B	109.9
C2—C1—C8	136.40 (19)	C14—C15—H15A	109.5
C6—C1—C8	106.57 (18)	C14—C15—H15B	109.5
C1—C2—O1	116.91 (18)	C14—C15—H15C	109.5
C3—C2—O1	122.3 (2)	H15A—C15—H15B	109.5
C3—C2—C1	120.6 (2)	H15A—C15—H15C	109.5
C2—C3—H3	119.8	H15B—C15—H15C	109.5
C2—C3—C4	120.3 (3)	O1—C13A—C14A	113.8 (8)
C4—C3—H3	119.8	O2A—C13A—O1	118.8 (11)
C3—C4—H4	119.1	O2A—C13A—C14A	125.2 (10)
C5—C4—C3	121.9 (2)	C13A—C14A—H14C	106.6
C5—C4—H4	119.1	C13A—C14A—H14D	106.6
C4—C5—H5	121.1	C13A—C14A—C15A	122.9 (16)
C4—C5—C6	117.8 (3)	H14C—C14A—H14D	106.6
C6—C5—H5	121.1	C15A—C14A—H14C	106.6
N1—C6—C1	107.88 (18)	C15A—C14A—H14D	106.6
N1—C6—C5	129.9 (2)	C14A—C15A—H15D	109.5
C5—C6—C1	122.3 (2)	C14A—C15A—H15E	109.5
N1—C7—H7	124.8	C14A—C15A—H15F	109.5
C8—C7—N1	110.4 (2)	H15D—C15A—H15E	109.5
C8—C7—H7	124.8	H15D—C15A—H15F	109.5
C1—C8—C9	128.71 (18)	H15E—C15A—H15F	109.5
C7—C8—C1	106.12 (17)	C19—O6—H6	110 (2)
C7—C8—C9	125.07 (18)	O3—C16—C17	121.3 (2)
C8—C9—H9A	109.8	O3—C16—C17A	91.4 (6)
C8—C9—H9B	109.8	O4—C16—O3	123.47 (18)
C8—C9—C10	109.36 (15)	O4—C16—C17	115.3 (2)
H9A—C9—H9B	108.3	O4—C16—C17A	144.0 (5)
C10—C9—H9A	109.8	O5—C19—O6	123.5 (2)

C10—C9—H9B	109.8	O5—C19—C18	119.8 (2)
N2—C10—C9	115.54 (16)	O5—C19—C18A	153.3 (5)
N2—C10—H10A	108.4	O6—C19—C18	116.7 (2)
N2—C10—H10B	108.4	O6—C19—C18A	81.7 (5)
C9—C10—H10A	108.4	C16—C17—H17	118.3
C9—C10—H10B	108.4	C18—C17—C16	123.3 (4)
H10A—C10—H10B	107.5	C18—C17—H17	118.3
N2—C11—H11A	109.5	C19—C18—H18	117.0
N2—C11—H11B	109.5	C17—C18—C19	125.9 (3)
N2—C11—H11C	109.5	C17—C18—H18	117.0
H11A—C11—H11B	109.5	C16—C17A—H17A	122.0
H11A—C11—H11C	109.5	C18A—C17A—C16	116.1 (14)
H11B—C11—H11C	109.5	C18A—C17A—H17A	122.0
N2—C12—H12A	109.5	C19—C18A—H18A	125.8
N2—C12—H12B	109.5	C17A—C18A—C19	108.4 (12)
N2—C12—H12C	109.5	C17A—C18A—H18A	125.8
O1—C2—C3—C4	174.8 (2)	C7—N1—C6—C5	179.3 (2)
O1—C13—C14—C15	-168.1 (13)	C7—C8—C9—C10	-79.5 (2)
O1—C13A—C14A—C15A	-161.9 (17)	C8—C1—C2—O1	4.8 (3)
N1—C7—C8—C1	0.6 (2)	C8—C1—C2—C3	-179.8 (2)
N1—C7—C8—C9	177.28 (17)	C8—C1—C6—N1	0.8 (2)
C1—C2—C3—C4	-0.3 (4)	C8—C1—C6—C5	-178.96 (19)
C1—C8—C9—C10	96.5 (2)	C8—C9—C10—N2	-176.14 (17)
C2—O1—C13—O2	21.1 (19)	C11—N2—C10—C9	65.0 (2)
C2—O1—C13—C14	-171.8 (7)	C12—N2—C10—C9	-62.5 (3)
C2—O1—C13A—O2A	-15.9 (19)	O2—C13—C14—C15	-1 (2)
C2—O1—C13A—C14A	-179.6 (9)	C13—O1—C2—C1	-128.1 (7)
C2—C1—C6—N1	-178.69 (17)	C13—O1—C2—C3	56.6 (8)
C2—C1—C6—C5	1.6 (3)	O2A—C13A—C14A—C15A	36 (3)
C2—C1—C8—C7	178.5 (2)	C13A—O1—C2—C1	-132.2 (7)
C2—C1—C8—C9	1.9 (4)	C13A—O1—C2—C3	52.6 (8)
C2—C3—C4—C5	0.2 (4)	O3—C16—C17—C18	-13.5 (4)

C3—C4—C5—C6	0.8 (4)	O3—C16—C17A—C18A	172.5 (11)
C4—C5—C6—N1	178.6 (2)	O4—C16—C17—C18	167.2 (3)
C4—C5—C6—C1	-1.7 (3)	O4—C16—C17A—C18A	-20.7 (17)
C6—N1—C7—C8	-0.1 (2)	O5—C19—C18—C17	172.5 (3)
C6—C1—C2—O1	-175.91 (17)	O5—C19—C18A—C17A	-28.3 (18)
C6—C1—C2—C3	-0.6 (3)	O6—C19—C18—C17	-7.6 (4)
C6—C1—C8—C7	-0.8 (2)	O6—C19—C18A—C17A	169.5 (10)
C6—C1—C8—C9	-177.38 (18)	C16—C17—C18—C19	-176.3 (2)
C7—N1—C6—C1	-0.5 (2)	C16—C17A—C18A—C19	-173.3 (7)

Table S11. *Hydrogen-bond geometry (Å, º) for 4-PrO-DMT hydrofumarate*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O4^{i}	0.84 (3)	2.02 (3)	2.810 (2)	156 (2)
N2—H2···O3	0.96 (3)	1.82 (3)	2.765 (2)	167 (2)
C9—H9*A*···O1	0.97	2.57	3.196 (3)	122
C10—H10*A*···O2^{ii}	0.97	2.34	3.302 (16)	171
C10—H10*A*···O2*A*^{ii}	0.97	2.23	3.147 (9)	158
C10—H10*B*···O5^{iii}	0.97	2.59	3.238 (3)	125
C12—H12*B*···O4	0.96	2.56	3.283 (3)	132
O6—H6···O3^{iv}	0.89 (1)	1.71 (1)	2.606 (2)	176 (3)

Symmetry codes: (i) *x*, *y*+1, *z*; (ii) -*x*+1, -*y*+1, -*z*+1; (iii) -*x*+1/2, *y*+1/2, -*z*+3/2; (iv) -*x*+1/2, *y*-1/2, -*z*+3/2.

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