Supporting information

Discovery and SAR of (R)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1H-benzo[d]azepine (lorcaserin), a selective serotonin 5-HT_{2C} receptor agonist for the treatment of obesity

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Table S1: Elemental analysis of key target compounds

Cmpd	Formula (HCl salt)	Calculated (HCl salt)	Calculated (HCl, hemihydrate)	Found
7d	$C_{11}H_{15}Cl_2N$	C, 56.91; H, 6.51; N, 6.03	C, 54.78; H, 6.69; N, 5.81	C, 54.83; H, 6.60; N, 5.77
7e	$C_{11}H_{15}Cl_2N$	C, 56.91; H, 6.51; N, 6.03	C, 54.78; H, 6.69; N, 5.81	C, 55.11; H, 6.69; N, 5.87
7g	$C_{12}H_{15}ClF_3N$	C, 54.24; H, 5.69; N, 5.27	C, 52.47; H, 5.87; N, 5.10	C, 53.91; H, 5.52; N, 5.12
7h	$C_{12}H_{15}ClF_3N$	C, 54.24; H, 5.69; N, 5.27	C, 52.47; H, 5.87; N, 5.10	C, 53.96; H, 5.56; N, 5.20
7q	$C_{11}H_{14}Cl_3N$	C, 49.56; H, 5.29; N, 5.25	C, 47.94; H, 5.49; ; N, 5.08	C, 48.46; H, 5.26; ; N, 5.05
7r	$C_{11}H_{14}Cl_3N$	C, 49.56; H, 5.29; N, 5.25	C, 47.94; H, 5.49; N, 5.08	C, 48.63; H, 5.32; N, 5.03
7u	$C_{12}H_{17}Cl_2NO$	C, 54.97; H, 6.54; N, 5.34;	C, 53.15; H, 6.69; N, 5.17	C, 51.12; H, 6.57; N, 4.85
7v	$C_{12}H_{17}Cl_2NO$	C, 54.97; H, 6.54; N, 5.34	C, 53.15; H, 6.69; N, 5.17	C, 51.52; H, 6.73; N, 4.89
7y	$C_{11}H_{14}Cl_3N$	C, 49.56; H, 5.29; N, 5.25	C, 47.94; H, 5.49; N, 5.08	C, 47.47; H, 5.16; N, 5.07
7z	$C_{11}H_{14}Cl_3N$	C, 49.56; H, 5.29; N, 5.25	C, 47.94; H, 5.49; N, 5.08	C, 49.43; H, 5.11; N, 5.10
7bb	$C_{11}H_{14}Cl_2FN$	C, 52.82; H, 5.64; N, 5.60	C, 50.98; H, 5.83; N, 5.40	C, 50.90; H, 5.62; N, 5.32

Lorcaserin hydrochloride absorbs water from the air to become lorcaserin hydrochloride hemihydrate. Other benzazepines may do the same.

Table S2: Crystal data and data collection parameters for lorcaserin hydrochloride hemihydrate

formula	$C_{11}H_{16}Cl_2NO_{0.50}$
formula weight	241.16
space group	$P2_12_12_1$ (No. 19)
a, Å	8.2368(13)
b, Å	11.508(4)
c, Å	26.552(7)
V, Å^3	2517(2)
Z	8
d_{calc}, g cm^{-3}	1.273
crystal dimensions, mm	0.60 x 0.28 x0.25
temperature, K	298
radiation (wavelength, Å)	Cu K_a (1.54184)
monochromator	graphite
linear abs coef, mm^{-1}	4.484
absorption correction applied	none
diffractometer	Nonius CÅD4
scan method	ω-2θ
h, k, l range	-10 to 10 -14 to 14 -32 to 32
2θ range, deg	5.02-140.00
scan width, deg	0.42 + 0.29tan(θ)
take-off angle, deg	3.00
programs used	SHELXTL
F_{000}	1048.0
weighting	$1/[\sigma^2(F_0^2)+(0.1028P)^2+0.3546P]$ where $P=(F_0^2+2F_c^2)/3$
data collected	5502
unique data	4749
R_{int}	0.026
data used in refinement	4749
cutoff used in *R*-factor calculations	$F_0^2>2.0\sigma(F_0^2)$
data with $I>2.0\sigma(I)$	4362
number of variables	288
largest shift/esd in final cycle	0.00
$R(F_0)$	0.056
$R_w(F_0^2)$	0.141
goodness of fit	1.098
absolute structure determination	*F*lack parameter (0.01(2))

Table S3: Positional parameters and their estimated standard deviations for lorcaserin hydrochloride hemihydrate

Atom	x	y	z	U(Å^2)
C1(3)	0.90680(10)	0.90059(7)	-0.31514(3)	0.0554(2)
C1(4)	0.46365(12)	0.71854(8)	-0.23258(3)	0.0678(3)
C1(18)	0.76517(16)	0.39163(11)	0.07719(4)	0.0862(3)
C1(28)	0.61066(18)	0.72235(9)	0.00097(5)	0.0961(4)
O(1W)	0.7624(4)	0.6494(3)	-0.29846(15)	0.0666(8)
N(13)	0.4479(4)	0.5026(3)	-0.16746(10)	0.0550(8)
N(23)	1.0228(4)	0.9703(2)	-0,20661(11)	0.0526(7)
C(11)	0.6339(5)	0.3366(3)	-0.14470(13)	0.0597(9)
C(12)	0.6102(5)	0.4473(3)	-0.17460(12)	0.0578(9)
C(14)	0.4048(4)	0.5403(3)	-0.11571(12)	0.0525(8)
C(15)	0.3841(4)	0.4404(3)	-0.07828(12)	0.0500(8)
C(16)	0.5478(3)	0.4019(2)	-0,05695(10)	0.0420(6)
C(17)	05813(4)	0.4138(2)	-0.00626(11)	0.0464(7)
C(18)	0.7300(4)	0.3793(3)	0.01285(12)	0.0534(8)
C(19)	0.8475(4)	0.3334(3)	-0.01836(14)	0.0599(9)
C(21)	1.0010(4)	0.7569(3)	-0.18882(11)	0.0511(8)
C(22)	1.1099(4)	0.8642(3)	-0.18930(14)	0.0555(9)
C(24)	0.8871(4)	1.0131(3)	-0.17496(14)	0.0574(9)
C(25)	0.7460(4)	0.9289(3)	-0.16979(15)	0.0562(8)
C(26)	0.7780(3)	0.8315(2)	-0.13192(12)	0.0453(7)
C(27)	0.6916(4)	0.8221(3)	-0.08706(14)	0.0577(9)
C(28)	0.7194(4)	0.7299(3)	-0.05485(13)	0.0560(9)
C(29)	0.8288(4)	0.6439(3)	-0.06619(12)	0.0492(8)
C(110)	0.8151(4)	0.3209(3)	-0.06858(14)	0.0593(9)
C(111)	0.6636(4)	0.3527(2)	-0.08907(12)	0.0495(8)
C(151)	0.2616(5)	0.4739(4)	-0.03805(17)	0.0746(12)
C(210)	0.9155(4)	0.6536(2)	-0.11052(11)	0.0464(7)
C(211)	0.8949(4)	0.7469(2)	-0.14296(11)	0.0414(6)
C(251)	0.5938(5)	1.0000(4)	-0.1569(2)	0.0973(18)
H(13A)	0.441(4)	0.557(3)	-0.1889(13)	0.044(8)*
H(13B)	0.370(6)	0.455(4)	-0.1792(16)	0.070(12)*
H(1W1)	1.254(8)	1.157(5)	-0.226(2)	0.09(2)*
H(1W2)	1.200(7)	1.220(5)	-0.1933(18)	0.085(15)*
H(231)	0.988(6)	0.961(4)	-0.2396(16)	0.066(11)*
H(232)	1.106(5)	1.037(3)	-0.2069(14)	0.058(10)*
H(15)	0.339	0.374	-0.097	0.060
H(17)	0.503	0.445	0.015	0.056
H(19)	0.948	0.311	-0.005	0.072
H(25)	0.728	0.893	-0.203	0.068
H(27)	0.615	0.878	-0.079	0.069
H(29)	0.844	0.581	-0.045	0.059
H(110)	0.895	0.291	-0.090	0.071

Table S3: Positional parameters and their estimated standard deviations for lorcaserin hydrochloride hemihydrate, continued

Atom	x	y	z	U(Å^2)
H(11A)	0538	0.288	-0.149	0.072
H(11B)	0.725	0.295	-0.159	0.072
H(12A)	0.693	0.502	-0.165	0.069
H(12B)	0.625	0.430	-0.210	0.069
H(14A)	0.304	0.584	-0.117	0.063
H(14B)	0.489	0.592	-0.103	0.063
H(15A)	0.254	0.413	-0.014	0.112
H(15B)	0.157	0.486	-0.053	0.112
H(15C)	0.296	0.544	-0.022	0.112
H(210)	0.990	0.596	-0.119	0.056
H(21A)	0.932	0.758	-0.218	0.061
H(21B)	1.069	0.688	-0.191	0.061
H(22A)	1.152	0.877	-0.156	0.067
H(22B)	1.202	0.850	-0.211	0.067
H(24A)	0.847	1.085	-0.189	0.069
H(24B)	0.929	1.030	-0.142	0.069
H(25A)	0.503	0.948	-0.152	0.146
H(25B)	0.571	1.053	-0.184	0.146
H(25C)	0.612	1.043	-0.126	0.146

Starred atoms were refined isotropically

Hydrogen atoms are included in calculation of structure factors but not refined

Figure S1: ORTEP drawing of lorcaserin