Supporting information

2-[(4-Phenylpiperazin-1-yl)methyl]imidazo(di)azines as Selective D_4-Ligands. Induction of Penile Erection by 2-[4-(2-methoxyphenyl)piperazin-1-ylmethyl]imidazo[1,2-*a*]pyridine (PIP3EA), a Potent and Selective D_4 Partial Agonist.

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X-ray diffraction. Crystals were grown by slow evaporation of methanol/chloroform solution at 293 K. The crystal used for x-ray measurement was lamellar, with dimensions: 0.05 x 0.28 x 0.38 mm. The studied compound, $C_{22}H_{22}O_{10}$, M_x = 566.50 g.mol^{-1} crystallizes in the orthorhombic system, space group P $2_12_12_1$ (Z = 4). The unit cell parameters are as follow: a = 10.0313(10), b = 14.78874(14) and c = 17.9853(16) Å with a cell volume of 2668.1(4) Å^3. The calculated density equal to 1.41 g.cm^{-3}. The linear absorption coefficient is μ = 0.106 mm^{-1} for the λ(MoK$_\alpha$) radiation (λ = 0.71073 Å).

The diffracted intensities were collected with an ENRAF NONIUS Kappa CCD diffractometer.

Structures were solved by Direct Methods (SHELXS 97)[52] and refined by full-matrix least squares against F^2 using SHELXL 97.[52] Scattering factors were taken from the International Tables for Crystallography.[53] All non-H atoms were refined anisotropically. H-atoms were fixed in calculated positions at parent C and O atoms, respectively. The final reliability factors are: R = 0.0438, wR = 0.0667 [I>2σ(I)] and the goodness of fit on F^2 was equal to 0.854. The minimum and maximum residual density was equal -0.129 and 0.144 e.Å^{-3} respectively. Crystal data, data collection parameters, and residual form refinement are summarized in Table 4. The fractional x, y, z coordinates and the equivalent Ueq thermal motion factors are listed in Table 5. The bond lengths and bond angles are given in Table 6 and 7 respectively. CCDC 604084 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

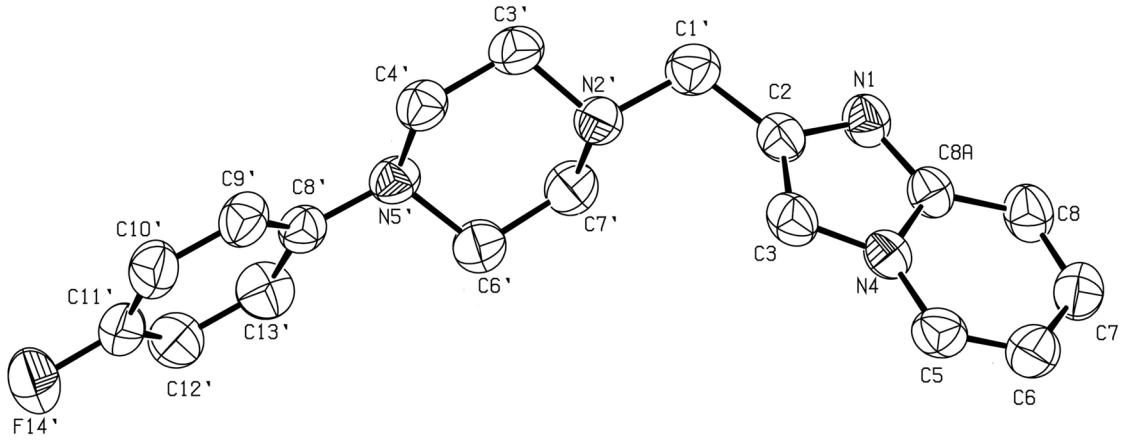

Figure 1. ORTEP for **3a**.

Table 1. Crystal data and structure refinement for **3a**.

Empirical formula	$C_{18}H_{19}FN_4$
Formula weight	310.37
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P21/c
Unit cell dimensions	a = 8.923(5) Å α = 90°.
	b = 16.000(5) Å β = 96.09(4)°.
	c = 11.308(6) Å γ = 90°.
Volume	1605.4(13)$Å^3$
Z, Calculated density	4, 1.284 Mg/m^3
Absorption coefficient	0.087 mm^{-1}
F(000)	656
Crystal size	0.40 x 0.20 x 0.05 mm
Theta range for data collection	2.21 to 24.99°.
Limiting indices	$-10 \leq h \leq 10$, $0 \leq k \leq 19$, $-13 \leq l \leq 13$
Reflections collected / unique	5141 / 2576 [R(int) = 0.0473]
Completeness to theta = 24.99	91.2 %
Absorption correction	Semi-empirical
Max. and min. transmission	0.9957 and 0.9661
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2576 / 0 / 209
Goodness-of-fit on F^2	0.955
Final R indices [I>2σ(I)]	R1 = 0.0389, ωR2 = 0.0697
R indices (all data)	R1 = 0.1111, ωR2 = 0.0869
Extinction coefficient	0.0023(6)
Largest diff. peak and hole	0.123 and -0.124 e. $Å^3$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **3a**.

	x	y	z	U(eq)
N(2')	2193(2)	1567(1)	47(2)	45(1)
F(14')	3387(2)	-2924(1)	-3407(1)	84(1)
N(5')	1923(2)	-62(1)	-1014(1)	45(1)
C(3')	1995(2)	825(2)	758(2)	53(1)
N(4)	3494(2)	4050(1)	-828(1)	43(1)
N(1)	1419(2)	3821(1)	83(2)	48(1)
C(1')	1723(2)	2319(2)	625(2)	55(1)
C(2)	2229(2)	3099(2)	60(2)	45(1)
C(8')	2324(2)	-797(2)	-1591(2)	44(1)
C(8A)	2189(2)	4396(2)	-463(2)	43(1)
C(7')	1352(3)	1432(2)	-1113(2)	58(1)
C(6')	1973(3)	702(2)	-1723(2)	59(1)
C(4')	2647(2)	71(1)	194(2)	48(1)
C(10')	3823(3)	-2049(2)	-1737(2)	60(1)
C(13')	1525(2)	-1024(2)	-2674(2)	57(1)
C(11')	3014(3)	-2229(2)	-2799(2)	58(1)
C(12')	1872(3)	-1730(2)	-3272(2)	60(1)
C(9')	3470(2)	-1334(2)	-1137(2)	53(1)
C(7)	2853(3)	5695(2)	-1290(2)	60(1)
C(5)	4490(2)	4520(2)	-1393(2)	53(1)
C(3)	3499(2)	3224(2)	-497(2)	51(1)
C(8)	1878(2)	5238(2)	-719(2)	55(1)
C(6)	4181(3)	5324(2)	-1621(2)	59(1)

Table 3. Bond lengths [Å] for **3a.**

N(2')-C(1')	1.453(3)
N(2')-C(3')	1.454(2)
N(2')-C(7')	1.456(3)
F(14')-C(11')	1.367(3)
N(5')-C(8')	1.410(3)
N(5')-C(4')	1.463(2)
N(5')-C(6')	1.464(3)
C(3')-C(4')	1.510(3)
C(3')-H(3'A)	0.9700
C(3')-H(3'B)	0.9700
N(4)-C(5)	1.373(3)
N(4)-C(3)	1.374(3)
N(4)-C(8A)	1.390(2)
N(1)-C(8A)	1.337(3)
N(1)-C(2)	1.364(2)
C(1')-C(2)	1.494(3)
C(1')-H(1'A)	0.9700
C(1')-H(1'B)	0.9700
C(2)-C(3)	1.368(3)
C(8')-C(9')	1.391(3)
C(8')-C(13')	1.398(3)
C(8A)-C(8)	1.400(3)
C(7')-C(6')	1.493(3)
C(7')-H(7'A)	0.9700
C(7')-H(7'B)	0.9700
C(6')-H(6'A)	0.9700
C(6')-H(6'B)	0.9700
C(4')-H(4'A)	0.9700

C(4')-H(4'B)	0.9700
C(10')-C(11')	1.364(3)
C(10')-C(9')	1.383(3)
C(10')-H(10')	0.9300
C(13')-C(12')	1.370(3)
C(13')-H(13')	0.9300
C(11')-C(12')	1.358(3)
C(12')-H(12')	0.9300
C(9')-H(9')	0.9300
C(7)-C(8)	1.352(3)
C(7)-C(6)	1.410(3)
C(7)-H(7)	0.9300
C(5)-C(6)	1.335(3)
C(5)-H(5)	0.9300
C(3)-H(3)	0.9300
C(8)-H(8)	0.9300
C(6)-H(6)	0.9300

Table 4. Bond angles [°] for **3a**.

C(1')-N(2')-C(3')	111.68(17)
C(1')-N(2')-C(7')	112.47(17)
C(3')-N(2')-C(7')	107.25(18)
C(8')-N(5')-C(4')	116.38(17)
C(8')-N(5')-C(6')	114.74(17)
C(4')-N(5')-C(6')	110.72(18)
N(2')-C(3')-C(4')	110.10(17)
N(2')-C(3')-H(3'A)	109.6
C(4')-C(3')-H(3'A)	109.6
N(2')-C(3')-H(3'B)	109.6
C(4')-C(3')-H(3'B)	109.6
H(3'A)-C(3')-H(3'B)	108.2
C(5)-N(4)-C(3)	132.07(19)
C(5)-N(4)-C(8A)	121.7(2)
C(3)-N(4)-C(8A)	106.26(18)
C(8A)-N(1)-C(2)	105.91(19)
N(2')-C(1')-C(2)	112.64(18)
N(2')-C(1')-H(1'A)	109.1
C(2)-C(1')-H(1'A)	109.1
N(2')-C(1')-H(1'B)	109.1
C(2)-C(1')-H(1'B)	109.1
H(1'A)-C(1')-H(1'B)	107.8
N(1)-C(2)-C(3)	110.6(2)
N(1)-C(2)-C(1')	120.94(19)
C(3)-C(2)-C(1')	128.4(2)
C(9')-C(8')-C(13')	116.7(2)
C(9')-C(8')-N(5')	123.9(2)
C(13')-C(8')-N(5')	119.4(2)

N(1)-C(8A)-N(4)	110.6(2)
N(1)-C(8A)-C(8)	131.1(2)
N(4)-C(8A)-C(8)	118.3(2)
N(2')-C(7')-C(6')	110.52(19)
N(2')-C(7')-H(7'A)	109.5
C(6')-C(7')-H(7'A)	109.5
N(2')-C(7')-H(7'B)	109.5
C(6')-C(7')-H(7'B)	109.5
H(7'A)-C(7')-H(7'B)	108.1
N(5')-C(6')-C(7')	111.45(18)
N(5')-C(6')-H(6'A)	109.3
C(7')-C(6')-H(6'A)	109.3
N(5')-C(6')-H(6'B)	109.3
C(7')-C(6')-H(6'B)	109.3
H(6'A)-C(6')-H(6'B)	108.0
N(5')-C(4')-C(3')	111.01(18)
N(5')-C(4')-H(4'A)	109.4
C(3')-C(4')-H(4'A)	109.4
N(5')-C(4')-H(4'B)	109.4
C(3')-C(4')-H(4'B)	109.4
H(4'A)-C(4')-H(4'B)	108.0
C(11')-C(10')-C(9')	118.6(2)
C(11')-C(10')-H(10')	120.7
C(9')-C(10')-H(10')	120.7
C(12')-C(13')-C(8')	121.7(2)
C(12')-C(13')-H(13')	119.2
C(8')-C(13')-H(13')	119.2
C(12')-C(11')-C(10')	121.9(2)
C(12')-C(11')-F(14')	119.5(2)

C(10')-C(11')-F(14')	118.6(2)
C(11')-C(12')-C(13')	119.3(2)
C(11')-C(12')-H(12')	120.3
C(13')-C(12')-H(12')	120.3
C(10')-C(9')-C(8')	121.8(2)
C(10')-C(9')-H(9')	119.1
C(8')-C(9')-H(9')	119.1
C(8)-C(7)-C(6)	120.1(2)
C(8)-C(7)-H(7)	120.0
C(6)-C(7)-H(7)	120.0
C(6)-C(5)-N(4)	119.1(2)
C(6)-C(5)-H(5)	120.4
N(4)-C(5)-H(5)	120.4
C(2)-C(3)-N(4)	106.7(2)
C(2)-C(3)-H(3)	126.7
N(4)-C(3)-H(3)	126.7
C(7)-C(8)-C(8A)	119.7(2)
C(7)-C(8)-H(8)	120.1
C(8A)-C(8)-H(8)	120.1
C(5)-C(6)-C(7)	121.0(2)
C(5)-C(6)-H(6)	119.5
C(7)-C(6)-H(6)	119.5

Purity Data

Elemental Analysis of Compounds

3a		C	H	N
	Calcd	69.66	6.17	18.05
	Found	69.57	6.19	17.89
3e		C	H	N
	Calcd	59.05	4.96	20.25
	Found	59.26	5.02	20.13
3i		C	H	N
	Calcd	65.58	5.83	22.49
	Found	65.67	5.72	22.63
3j		C	H	N
	Calcd	65.58	5.83	22.49
	Found	65.74	5.82	22.54
3b		C	H	N
	Calcd	59.84	5.02	15.51
	Found	59.81	5.13	15.43
3c		C	H	N
	Calcd	70.78	6.88	17.38
	Found	70.85	6.93	17.54
3d		C	H	N
	Calcd	66.15	5.86	17.14
	Found	66.28	5.93	17.27
3f		C	H	N
	Calcd	51.47	4.07	17.65
	Found	51.69	4.12	17.67
3g		C	H	N
	Calcd	60.42	5.63	19.57
	Found	60.51	5.59	19.48
3h		C	H	N
	Calcd	56.36	4.73	19.33
	Found	56.32	4.81	19.56
4a		C	H	N
	Calcd	59.33	5.88	18.87
	Found	59.41	5.73	18.92
4b		C	H	N
	Calcd	57.39	5.91	21.30
	Found	57.56	6.02	21.28
7a		C	H	N
	Calcd	56.87	5.27	13.96
	Found	56.94	5.36	13.81
7b		C	H	N
	Calcd	50.90	4.72	12.50
	Found	50.86	4.81	12.67
7c		C	H	N
	Calcd	51.84	5.58	13.49
	Found	51.96	5.51	13.67

7d		C	H	N
	Calcd	51.96	5.01	12.12
	Found	52.03	5.16	12.29
7e		C	H	N
	Calcd	49.12	3.89	12.73
	Found	49.37	4.11	12.66
8a		C	H	N
	Calcd	69.78	6.41	19.38
	Found	69.81	6.52	19.34
8b		C	H	N
	Calcd	68.38	7.41	16.61
	Found	68.49	7.38	16.82
8c		C	H	N
	Calcd	68.63	6.51	20.88
	Found	68.73	6.67	20.72
8d		C	H	N
	Calcd	68.02	6.23	21.63
	Found	68.22	6.15	21.68
8e		C	H	N
	Calcd	75.70	6.84	13.58
	Found	75.81	6.79	13.64