SUPPORTING INFORMATION

Discovery and SAR of Novel 2,3-Dihydrobenzofuran-7-carboxamide and 2,3-Dihydrobenzofuran-3(2H)-one-7-carboxamide Derivatives as Poly(ADP-ribose)polymerase-1 Inhibitors

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Table S1. Crystal parameters for Co-crystal of (-)-**13c**-, **59**- and **65**-PARP-1

Data Collection	**(-)-13c**	**59**	**65**
PDB ID	**4OPX**	**4OQA**	**4OQB**
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Unit cell dimensions	*a*=65.150, *b*=112.910, *c*=295.290	*a*=65.160, *b*=114.230, *c*=294.240	*a*=65.100, *b*=113.080, *c*=296.230
Wavelength (Å)	1.075	1.075	1.075
Resolution range (Å)	50---3.31	50---3.65	50---3.36
Reflections	196,196 (31,324)	148,736 (23,707)	186,164 (29,853)
No. of unique reflections	33,094 (5220)	24,945 (3895)	31,790 (5035)
Rmeas (%)	11.2 (175.4)	7.7 (176.4)	11.1 (170.2)
Completeness (%)	99.2 (98.7)	98.4 (98.0)	99.0 (99.3)
Redundancy	5.9 (6.0)	6.0 (6.1)	5.9 (5.9)
CC1/2	99.9 (63.6)	99.9 (51.1)	99.9 (37.3)
Mean I / σ(I)	0.96	1.15	1.11
Model Refinement			
Resolution (Å)	20---3.3132	20---3.6470	20---3.3621
Rcrystal (%)	0.3038	0.3002	0.3231
Rfree (%)	0.3248	0.3342	0.349
R.m.s.d. for bond length (Å)	0.004	0.004	0.004
R.m.s.d. for bond angles (°)	0.7658	0.774	0.7681
Ramachandran plot (%)			
Most favored	95.28 (1273)	94.99 (1269)	94.84 (1267)
Allowed	100 (1338)	100 (1338)	100 (1338)

Table S2. Crystal data and structure refinement for diastereomeric salt of (*R*)-(-)-**12a** with (*S*)-(-)-α-methylbenzylamine

Identification code	Table S2	
Empirical formula	$C_{18}H_{21}NO_3$	
Formula weight	299.36	
Temperature	90.0(5) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 10.2720(4) Å	α= 90°
	b = 7.0135(3) Å	β= 111.298(2)°
	c = 11.5362(4) Å	γ = 90°
Volume	774.34(5) $Å^3$	
Z	2	
Density (calculated)	1.284 Mg/m^3	
Absorption coefficient	0.702 mm^{-1}	
F(000)	320	
Crystal size	0.22 x 0.12 x 0.09 mm^3	
Theta range for data collection	4.11 to 68.81°	
Index ranges	-12<=h<=11, -8<=k<=8, -13<=l<=13	
Reflections collected	13226	
Independent reflections	2739 [R(int) = 0.0305]	
Completeness to theta = 67.00∞	99.6%	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.796
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2739 / 1 / 210
Goodness-of-fit on F^2	1.087
Final R indices [I>2sigma(I)]	R1 = 0.0252, wR2 = 0.0628
R indices (all data)	R1 = 0.0268, wR2 = 0.0638
Absolute structure parameter	-0.12(15)
Largest diff. peak and hole	0.223 and -0.131 e.$Å^{-3}$

Table S3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Table S2. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	3886(1)	6667(1)	6294(1)	22(1)
O(2)	1625(1)	3995(1)	5450(1)	19(1)
O(3)	2306(1)	1065(1)	6143(1)	24(1)
C(1)	4340(1)	5359(2)	7232(1)	18(1)
C(2)	3701(1)	3611(2)	7246(1)	18(1)
C(3)	4318(1)	2491(2)	8316(1)	22(1)
C(4)	5492(2)	3077(2)	9296(1)	26(1)
C(5)	6128(2)	4801(2)	9233(1)	24(1)
C(6)	5548(1)	5935(2)	8198(1)	21(1)
C(7)	5969(2)	7860(2)	7882(1)	28(1)
C(8)	4961(1)	8160(2)	6528(1)	24(1)
C(9)	5653(2)	7916(2)	5590(1)	30(1)
C(10)	2453(1)	2835(2)	6204(1)	17(1)
N(1)	-939(1)	2554(2)	3949(1)	17(1)
C(11)	921(1)	151(2)	3085(1)	25(1)
C(12)	1623(2)	-1261(2)	2709(2)	30(1)
C(13)	1026(2)	-2103(2)	1549(1)	27(1)
C(14)	-302(2)	-1564(2)	781(1)	26(1)

C(15)	-1010(2)	-163(2)	1162(1)	24(1)
C(16)	-401(1)	732(2)	2305(1)	21(1)
C(17)	-1112(1)	2447(2)	2606(1)	20(1)
C(18)	-548(2)	4272(2)	2256(1)	25(1)

Table S4. Bond lengths [Å] and angles [°] for Table S2

O(1)-C(1)	1.3656(16)
O(1)-C(8)	1.4737(17)
O(2)-C(10)	1.2666(16)
O(3)-C(10)	1.2488(17)
C(1)-C(6)	1.3927(18)
C(1)-C(2)	1.3936(19)
C(2)-C(3)	1.4052(19)
C(2)-C(10)	1.5050(18)
C(3)-C(4)	1.382(2)
C(3)-H(3)	0.9500
C(4)-C(5)	1.389(2)
C(4)-H(4)	0.9500
C(5)-C(6)	1.378(2)
C(5)-H(5)	0.9500
C(6)-C(7)	1.502(2)
C(7)-C(8)	1.543(2)
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(8)-C(9)	1.505(2)
C(8)-H(8)	1.0000
C(9)-H(9A)	0.9800

C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
N(1)-C(17)	1.4959(16)
N(1)-H(1N)	0.956(18)
N(1)-H(2N)	0.919(18)
N(1)-H(3N)	0.935(17)
C(11)-C(12)	1.385(2)
C(11)-C(16)	1.389(2)
C(11)-H(11)	0.9500
C(12)-C(13)	1.385(2)
C(12)-H(12)	0.9500
C(13)-C(14)	1.382(2)
C(13)-H(13)	0.9500
C(14)-C(15)	1.386(2)
C(14)-H(14)	0.9500
C(15)-C(16)	1.387(2)
C(15)-H(15)	0.9500
C(16)-C(17)	1.5116(19)
C(17)-C(18)	1.5186(19)
C(17)-H(17)	1.0000
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800

C(1)-O(1)-C(8)	108.33(10)
O(1)-C(1)-C(6)	112.81(12)
O(1)-C(1)-C(2)	125.01(11)
C(6)-C(1)-C(2)	122.17(12)
C(1)-C(2)-C(3)	115.96(12)
C(1)-C(2)-C(10)	125.24(12)
C(3)-C(2)-C(10)	118.77(12)
C(4)-C(3)-C(2)	122.24(14)
C(4)-C(3)-H(3)	118.9
C(2)-C(3)-H(3)	118.9
C(3)-C(4)-C(5)	120.26(13)
C(3)-C(4)-H(4)	119.9
C(5)-C(4)-H(4)	119.9
C(6)-C(5)-C(4)	118.94(13)
C(6)-C(5)-H(5)	120.5
C(4)-C(5)-H(5)	120.5
C(5)-C(6)-C(1)	120.36(13)
C(5)-C(6)-C(7)	131.08(13)
C(1)-C(6)-C(7)	108.54(12)
C(6)-C(7)-C(8)	102.81(11)
C(6)-C(7)-H(7A)	111.2
C(8)-C(7)-H(7A)	111.2

C(6)-C(7)-H(7B)	111.2
C(8)-C(7)-H(7B)	111.2
H(7A)-C(7)-H(7B)	109.1
O(1)-C(8)-C(9)	107.78(12)
O(1)-C(8)-C(7)	105.75(11)
C(9)-C(8)-C(7)	113.21(12)
O(1)-C(8)-H(8)	110.0
C(9)-C(8)-H(8)	110.0
C(7)-C(8)-H(8)	110.0
C(8)-C(9)-H(9A)	109.5
C(8)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(8)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
O(3)-C(10)-O(2)	124.21(12)
O(3)-C(10)-C(2)	117.07(12)
O(2)-C(10)-C(2)	118.71(12)
C(17)-N(1)-H(1N)	112.3(10)
C(17)-N(1)-H(2N)	110.8(10)
H(1N)-N(1)-H(2N)	108.2(13)
C(17)-N(1)-H(3N)	113.7(9)
H(1N)-N(1)-H(3N)	107.8(13)

H(2N)-N(1)-H(3N)	103.6(14)
C(12)-C(11)-C(16)	120.30(13)
C(12)-C(11)-H(11)	119.9
C(16)-C(11)-H(11)	119.9
C(11)-C(12)-C(13)	120.60(14)
C(11)-C(12)-H(12)	119.7
C(13)-C(12)-H(12)	119.7
C(14)-C(13)-C(12)	119.39(14)
C(14)-C(13)-H(13)	120.3
C(12)-C(13)-H(13)	120.3
C(13)-C(14)-C(15)	119.95(13)
C(13)-C(14)-H(14)	120.0
C(15)-C(14)-H(14)	120.0
C(14)-C(15)-C(16)	121.03(13)
C(14)-C(15)-H(15)	119.5
C(16)-C(15)-H(15)	119.5
C(15)-C(16)-C(11)	118.69(13)
C(15)-C(16)-C(17)	119.28(12)
C(11)-C(16)-C(17)	121.65(12)
N(1)-C(17)-C(16)	113.05(11)
N(1)-C(17)-C(18)	108.64(11)
C(16)-C(17)-C(18)	110.33(10)
N(1)-C(17)-H(17)	108.2

C(16)-C(17)-H(17)	108.2
C(18)-C(17)-H(17)	108.2
C(17)-C(18)-H(18A)	109.5
C(17)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(17)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5

Table S5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Table S2. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	22(1)	19(1)	24(1)	2(1)	7(1)	-4(1)
O(2)	18(1)	16(1)	23(1)	-1(1)	6(1)	2(1)
O(3)	26(1)	14(1)	30(1)	0(1)	9(1)	-2(1)
C(1)	19(1)	18(1)	19(1)	-1(1)	10(1)	3(1)
C(2)	19(1)	16(1)	22(1)	-1(1)	12(1)	2(1)
C(3)	25(1)	19(1)	24(1)	1(1)	11(1)	2(1)
C(4)	27(1)	29(1)	21(1)	4(1)	8(1)	5(1)
C(5)	21(1)	32(1)	19(1)	-5(1)	6(1)	1(1)
C(6)	20(1)	22(1)	23(1)	-7(1)	10(1)	-2(1)
C(7)	24(1)	27(1)	31(1)	-5(1)	9(1)	-8(1)
C(8)	22(1)	17(1)	35(1)	0(1)	11(1)	-4(1)
C(9)	25(1)	31(1)	35(1)	5(1)	12(1)	-1(1)
C(10)	19(1)	16(1)	20(1)	-2(1)	11(1)	1(1)
N(1)	18(1)	15(1)	20(1)	0(1)	8(1)	0(1)
C(11)	22(1)	25(1)	27(1)	-7(1)	8(1)	-3(1)
C(12)	21(1)	29(1)	40(1)	-5(1)	11(1)	1(1)
C(13)	33(1)	20(1)	37(1)	-5(1)	22(1)	-4(1)
C(14)	38(1)	22(1)	22(1)	-3(1)	16(1)	-5(1)

C(15)	29(1)	23(1)	21(1)	3(1)	9(1)	-2(1)
C(16)	23(1)	18(1)	24(1)	3(1)	13(1)	-4(1)
C(17)	19(1)	22(1)	19(1)	1(1)	6(1)	-1(1)
C(18)	32(1)	21(1)	27(1)	5(1)	15(1)	2(1)

Table S6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3)

for Table S2

	x	y	z	U(eq)
H(3)	3915	1290	8368	27
H(4)	5865	2298	10015	31
H(5)	6951	5192	9894	29
H(7A)	6954	7861	7940	33
H(7B)	5842	8859	8438	33
H(8)	4519	9449	6437	29
H(9A)	6128	6679	5716	44
H(9B)	6338	8938	5695	44
H(9C)	4945	7974	4748	44
H(1N)	-1234(16)	1410(30)	4233(14)	26
H(2N)	-1441(17)	3560(30)	4086(15)	26
H(3N)	-23(17)	2810(20)	4480(14)	26
H(11)	1344	724	3880	30
H(12)	2524	-1656	3251	36
H(13)	1523	-3043	1284	32
H(14)	-730	-2154	-9	31
H(15)	-1926	191	633	29

H(17)	-2133	2367	2099	24
H(18A)	-1039	5370	2429	38
H(18B)	-694	4246	1368	38
H(18C)	454	4379	2745	38

Table S7. Torsion angles [°] for Table S2

C(8)-O(1)-C(1)-C(6)	8.58(14)
C(8)-O(1)-C(1)-C(2)	-170.70(12)
O(1)-C(1)-C(2)-C(3)	-178.54(12)
C(6)-C(1)-C(2)-C(3)	2.25(18)
O(1)-C(1)-C(2)-C(10)	3.41(19)
C(6)-C(1)-C(2)-C(10)	-175.80(12)
C(1)-C(2)-C(3)-C(4)	-0.26(19)
C(10)-C(2)-C(3)-C(4)	177.92(12)
C(2)-C(3)-C(4)-C(5)	-1.8(2)
C(3)-C(4)-C(5)-C(6)	1.9(2)
C(4)-C(5)-C(6)-C(1)	0.08(19)
C(4)-C(5)-C(6)-C(7)	178.31(13)
O(1)-C(1)-C(6)-C(5)	178.49(12)
C(2)-C(1)-C(6)-C(5)	-2.22(19)
O(1)-C(1)-C(6)-C(7)	-0.11(15)
C(2)-C(1)-C(6)-C(7)	179.19(11)
C(5)-C(6)-C(7)-C(8)	173.80(14)
C(1)-C(6)-C(7)-C(8)	-7.81(14)
C(1)-O(1)-C(8)-C(9)	108.25(12)
C(1)-O(1)-C(8)-C(7)	-13.11(14)
C(6)-C(7)-C(8)-O(1)	12.40(14)

C(6)-C(7)-C(8)-C(9)	-105.39(13)
C(1)-C(2)-C(10)-O(3)	154.88(12)
C(3)-C(2)-C(10)-O(3)	-23.12(17)
C(1)-C(2)-C(10)-O(2)	-25.09(18)
C(3)-C(2)-C(10)-O(2)	156.91(12)
C(16)-C(11)-C(12)-C(13)	0.5(2)
C(11)-C(12)-C(13)-C(14)	-2.0(2)
C(12)-C(13)-C(14)-C(15)	1.4(2)
C(13)-C(14)-C(15)-C(16)	0.7(2)
C(14)-C(15)-C(16)-C(11)	-2.2(2)
C(14)-C(15)-C(16)-C(17)	170.90(12)
C(12)-C(11)-C(16)-C(15)	1.6(2)
C(12)-C(11)-C(16)-C(17)	-171.29(13)
C(15)-C(16)-C(17)-N(1)	145.15(12)
C(11)-C(16)-C(17)-N(1)	-41.99(17)
C(15)-C(16)-C(17)-C(18)	-92.98(14)
C(11)-C(16)-C(17)-C(18)	79.88(15)

Table S8. Hydrogen bonds for Table S2 [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N)...O(2)#1	0.956(18)	1.810(19)	2.7503(15)	167.3(15)
N(1)-H(2N)...O(3)#2	0.919(18)	1.946(19)	2.8182(16)	157.7(14)
N(1)-H(3N)...O(2)	0.935(17)	1.853(17)	2.7648(14)	164.4(15)