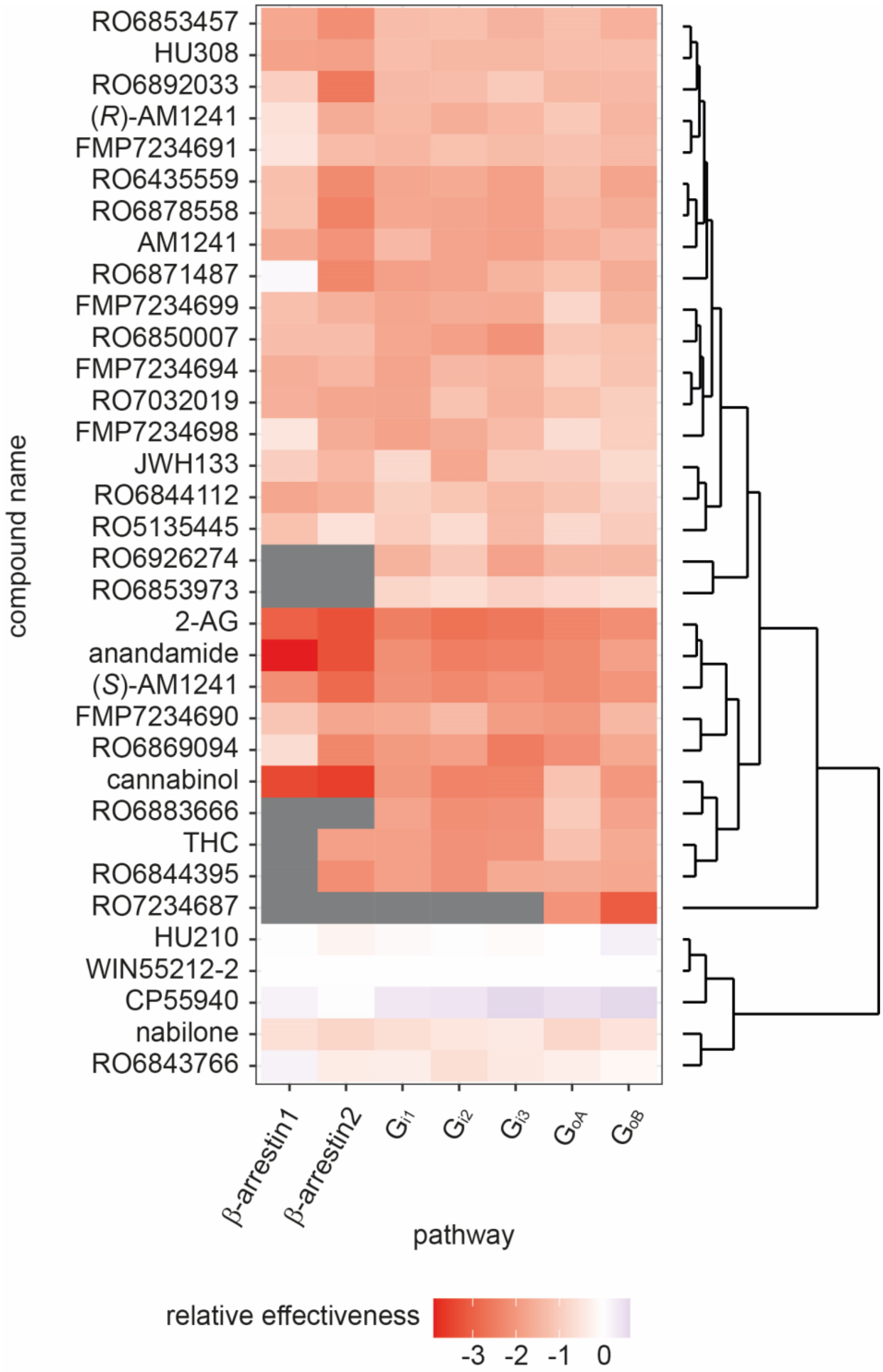
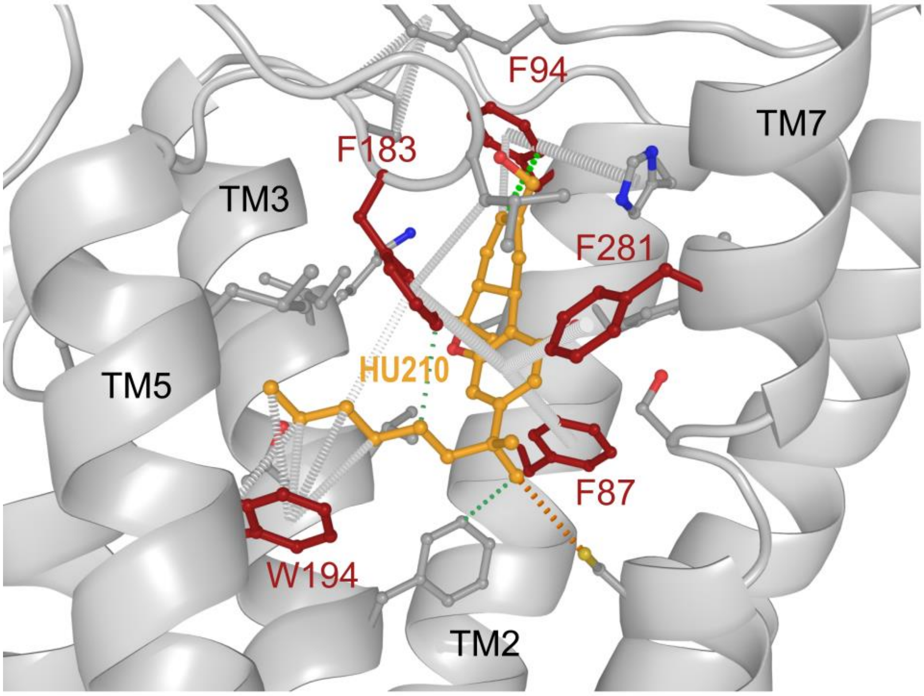


Figure S1. Ligand relative effectiveness (RE) on CB2 signaling represented as a heat map. Data from Table S16. For several ligands logR did not converge and RE could not be determined (grey). Three main clusters are observed, one having similar signaling properties as the reference ligand WIN55212-2, another with signaling reduced more or less uniform across the observed signaling pathways, and the third group where β-arrestin signaling was affected more strongly compared to G protein signaling.



residue	no. of interactions*
25	0
87	16
90	0
91	0
94	9
95	1
109	0
110	3
113	5
114	2
117	6
182	1
183	22
184	1
190	1
191	1
194	16
261	1
265	5
281	7
282	0
285	1
288	2

Figure S2. Interactions between CB2 receptor and HU210 ligand, as calculated using Arpeggio server. HU210 is shown in orange sticks and CB2 residues forming the highest number of specific interactions with ligand in red. Specific interactions include pi-pi stacking (grey), hydrophobic-van der Waals (green) and weak polar-van der Waals (orange). Table shows all residues found to contact HU210, while in red are highlighted residues forming the highest number of specific interactions.

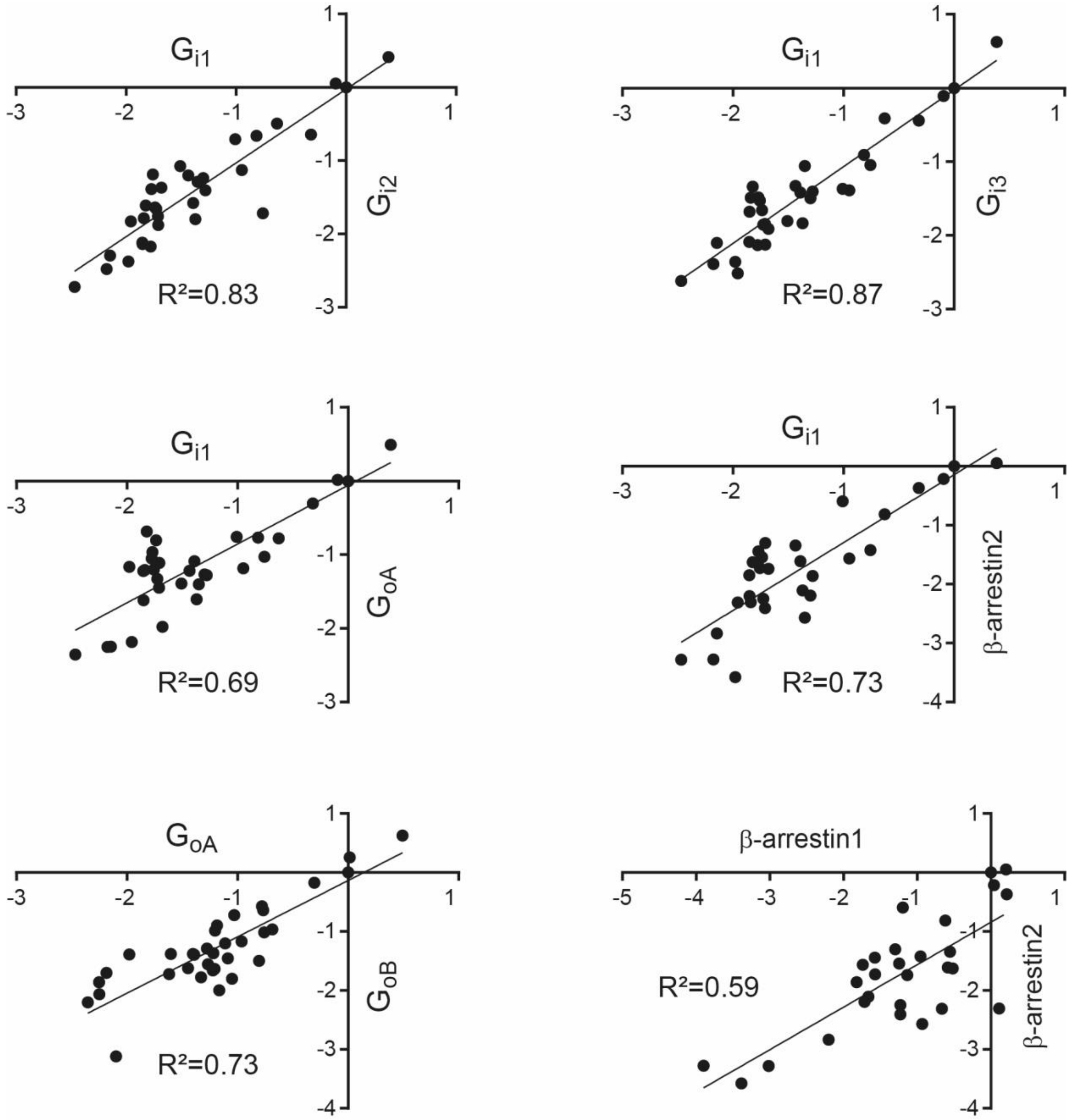


Figure S3. Correlation of ligand relative effectiveness (RE) data on CB2 signaling across the pathways. Data from Table S16. While strong correlation was observed among G_i family members, somewhat reduced correlation was observed between G_i vs. G_o, G_i vs. β-arrestin and among G_o family responses. The weakest correlation was observed between the two β-arrestin responses.

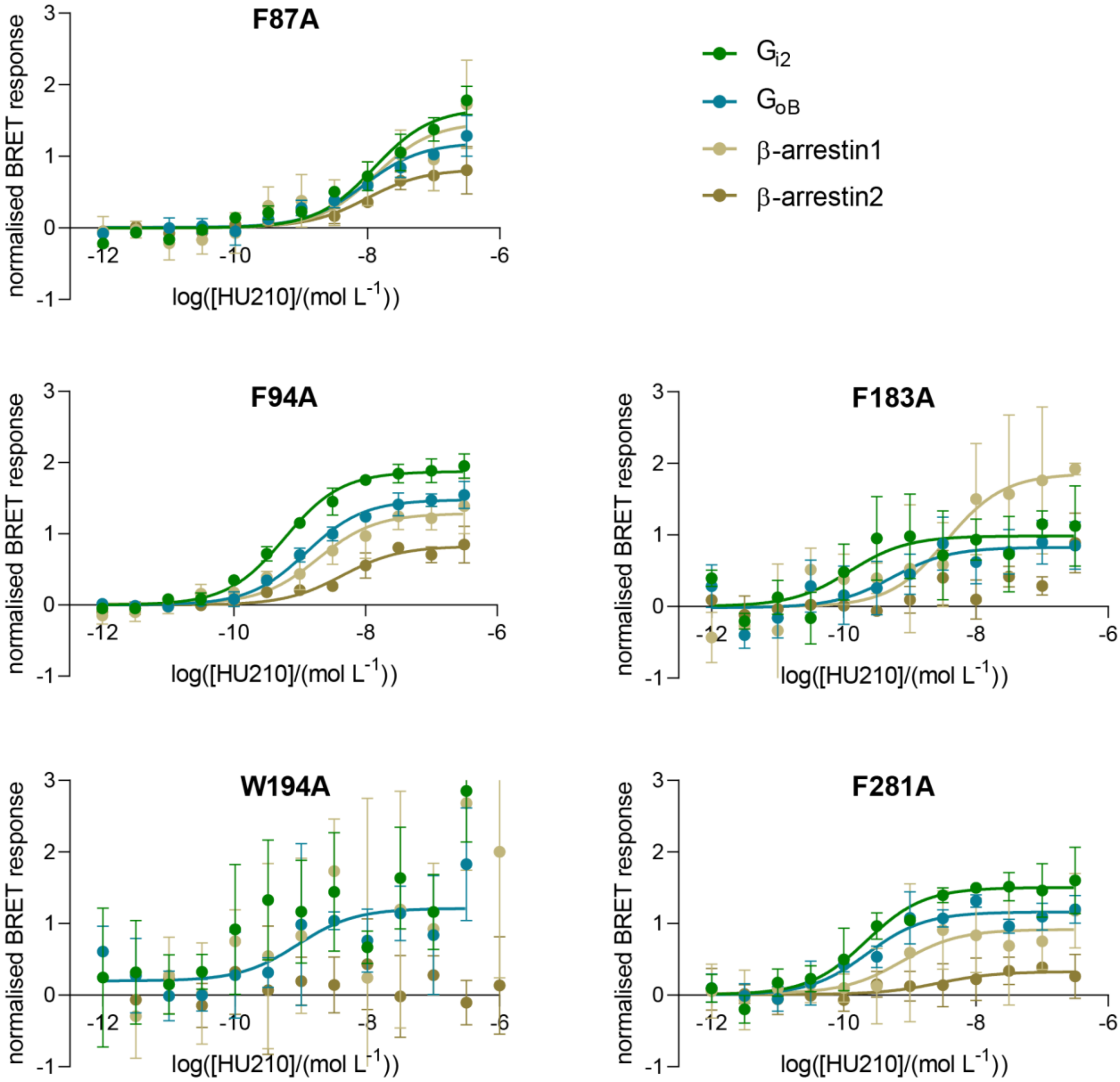


Figure S4. Concentration-dependent activation of G proteins and β-arrestins mediated by single amino acid CB2 mutants F87A, F94A, F183A, W194A and F281A upon stimulation with agonist HU210. Signal response was corrected for expression levels of the mutants and normalized to the wild type receptor response.

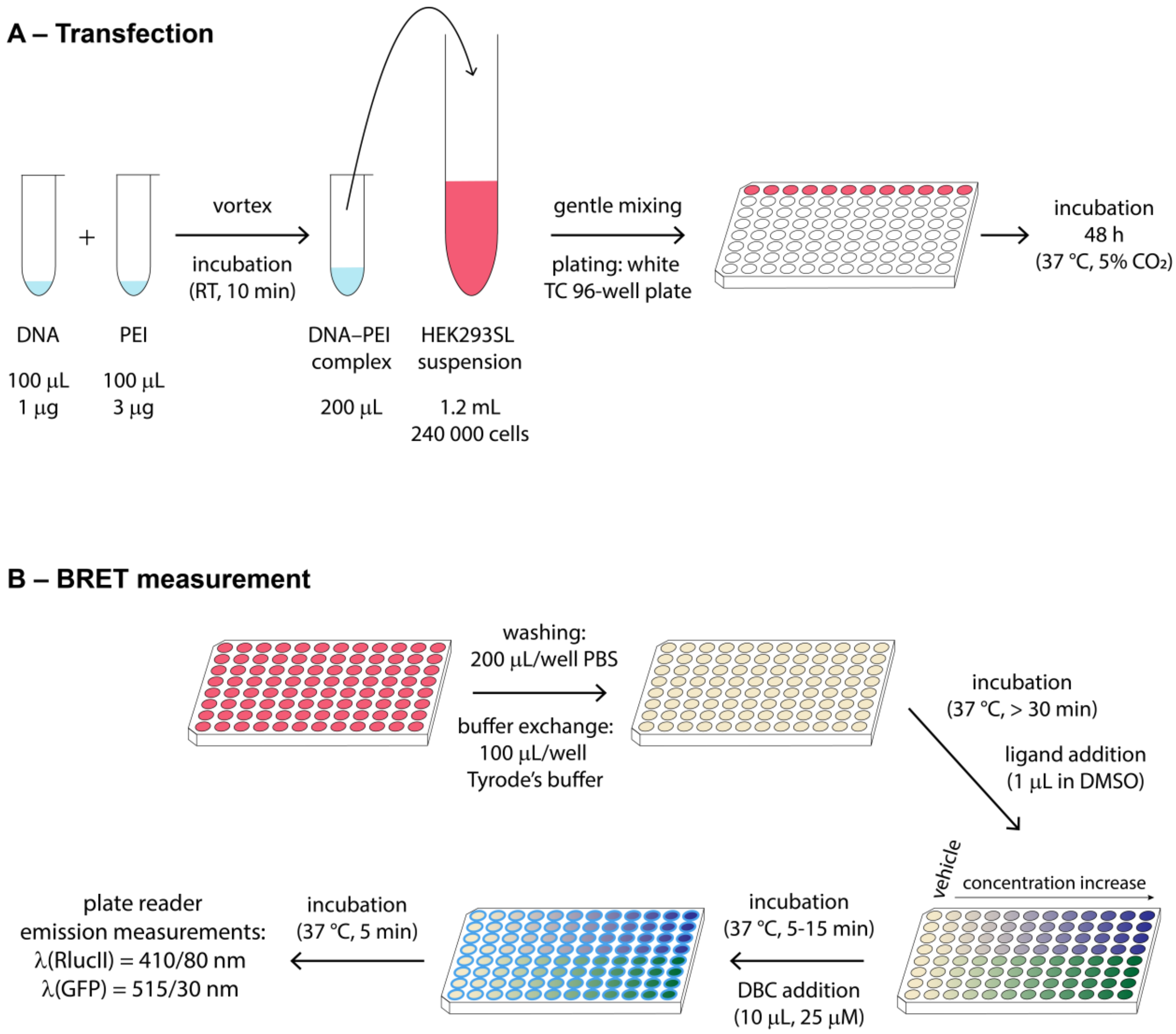
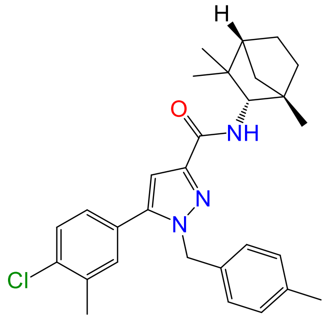
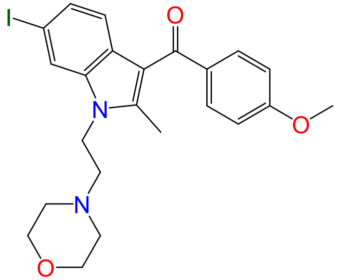
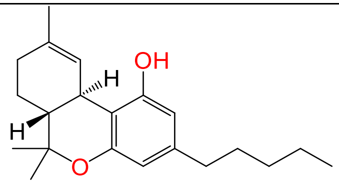
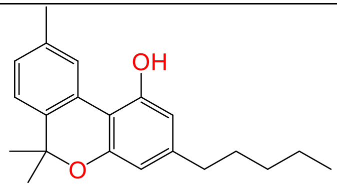
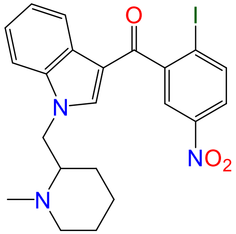
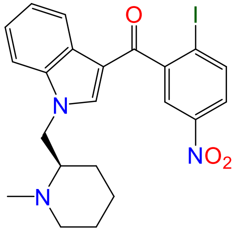
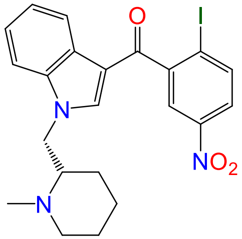
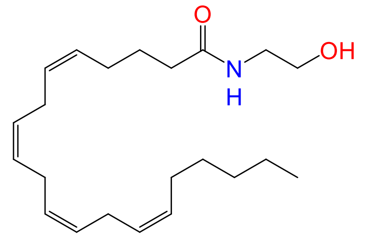
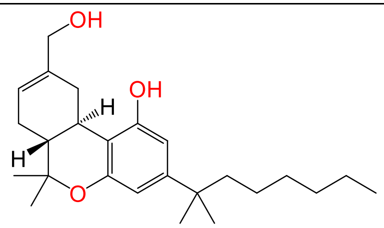
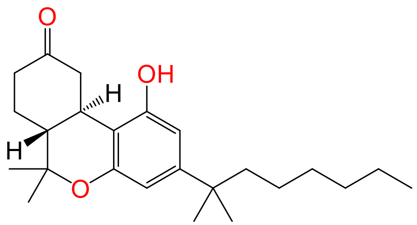
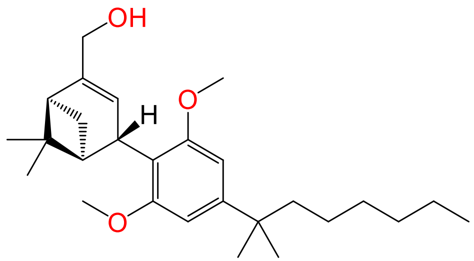


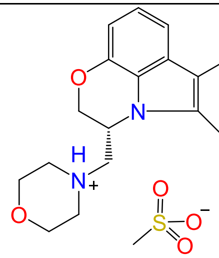
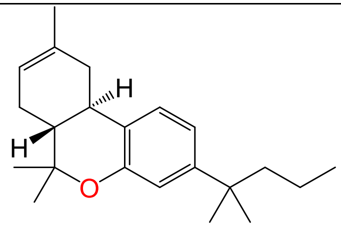
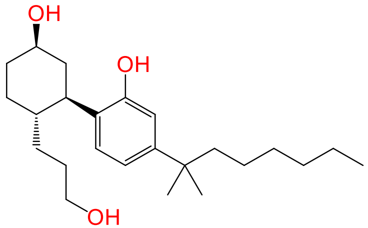
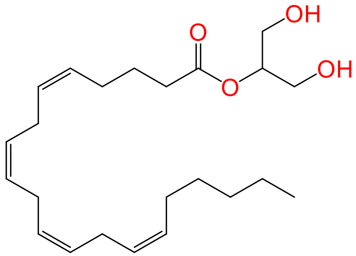
Figure S5. Schematic representation of transfection (A) and BRET measurement (B) protocols as described in Materials and Methods.

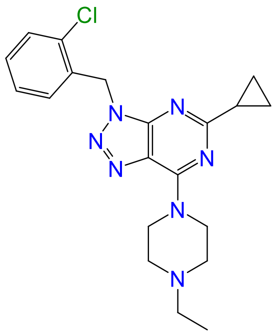
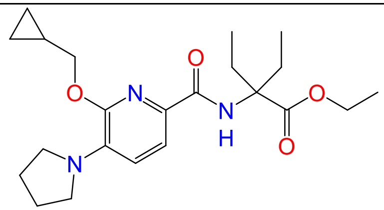
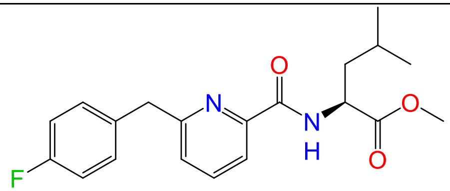
Table S1. Chemical structures, IUPAC names and CAS numbers of the cannabinoid receptor ligands used in the biased signaling studies.

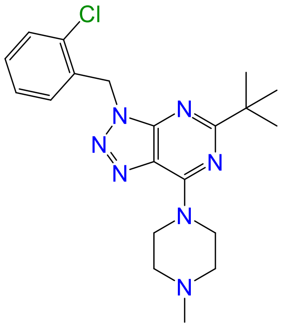
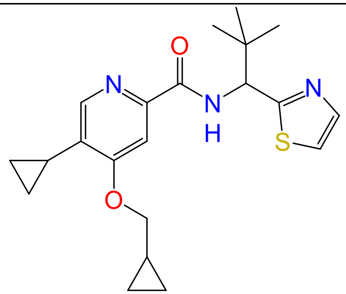
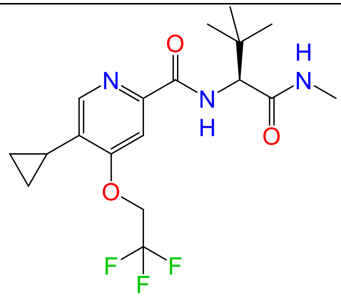
Compound	Chemical structure	IUPAC name	CAS number
SR144528		5-(4-Chloro-3-methylphenyl)-1-[(4-methylphenyl)methyl]-N-[(1S,2S,4R)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-yl]-1H-pyrazole-3-carboxamide	192703-06-3
AM630		{6-Iodo-2-methyl-1-[2-(morpholin-4-yl)ethyl]-1H-indol-3-yl}(4-methoxyphenyl)methanone	164178-33-0
THC		(-)-(6aR,10aR)-6,6,9-Trimethyl-3-pentyl-6a,7,8,10a-tetrahydro-6H-dibenzo[b,d]pyran-1-ol	1972-08-3

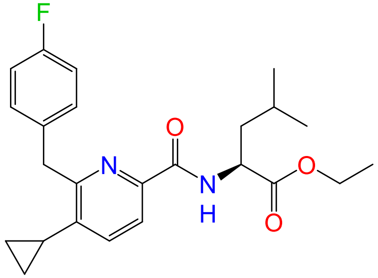
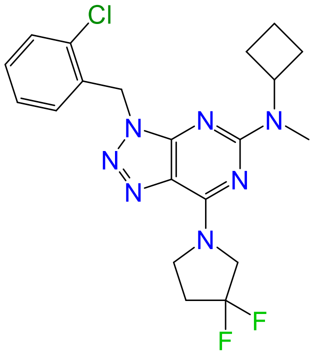
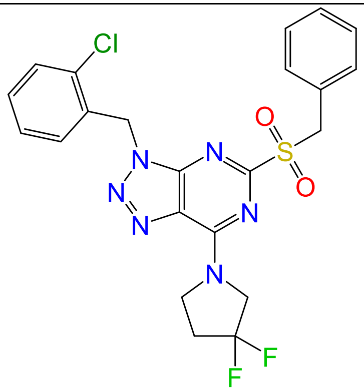
cannabinol		6,6,9-Trimethyl-3-pentyl-6H-dibenzo[b,d]pyran-1-ol	521-35-7
(*rac*)-AM1241		(2-Iodo-5-nitrophenyl){1-[(1-methylpiperidin-2-yl)methyl]-1H-indol-3-yl}methanone	444912-48-5
(*R*)-AM1241		(2-Iodo-5-nitrophenyl)(1-{[(2R)-1-methylpiperidin-2-yl]methyl}-1H-indol-3-yl)methanone	444912-51-0
(*S*)-AM1241		(2-Iodo-5-nitrophenyl)(1-{[(2S)-1-methylpiperidin-2-yl]methyl}-1H-indol-3-yl)methanone	444912-53-2

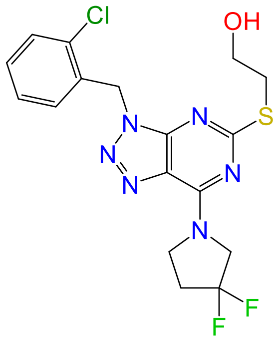
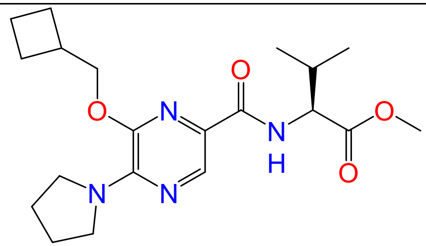
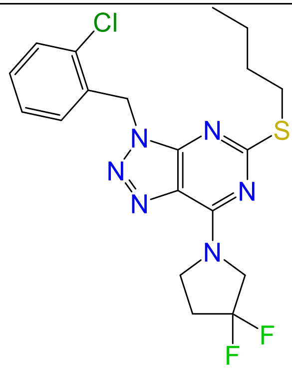
anandamide		(5Z,8Z,11Z,14Z)-N-(2-Hydroxyethyl)eicosa-5,8,11,14-tetraenamide	94421-68-8
HU210		(6aR,10aR)-9-(Hydroxymethyl)-6,6-dimethyl-3-(2-methyloctan-2-yl)-6a,7,10,10a-tetrahydro-6H-dibenzo[b,d]pyran-1-ol	112830-95-2
nabilone		(6aR,10aR)-1-Hydroxy-6,6-dimethyl-3-(2-methyloctan-2-yl)-6,6a,7,8,10,10a-hexahydro-9H-dibenzo[b,d]pyran-9-one	51022-71-0
HU308		{(1S,4S,5S)-4-[2,6-Dimethoxy-4-(2-methyloctan-2-yl)phenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl}methanol	256934-39-1

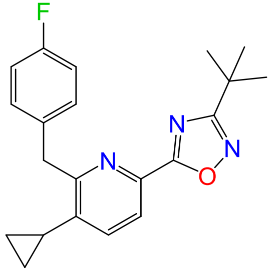
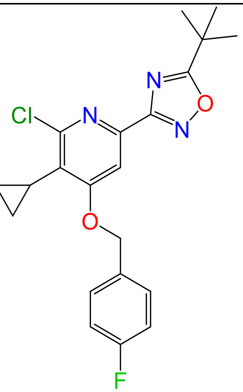
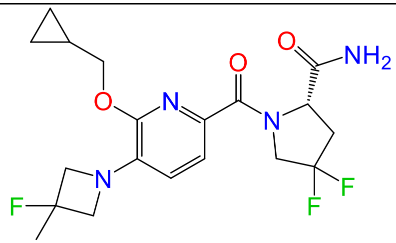
WIN55212-2		Methanesulfonic acid--{(3R)-5-methyl-3-[(morpholin-4-yl)methyl]-2,3-dihydro[1,4]oxazino[2,3,4-hi]indol-6-yl}(naphthalen-1-yl)methanone (1/1)	131543-23-2
JWH133		(6aR,10aR)-6,6,9-Trimethyl-3-(2-methylpentan-2-yl)-6a,7,10,10a-tetrahydro-6H-dibenzo[b,d]pyran	259869-55-1
CP55940		2-[(1R,2R,5R)-5-Hydroxy-2-(3-hydroxypropyl)cyclohexyl]-5-(2-methyloctan-2-yl)phenol	83002-04-4
2-AG		1,3-Dihydroxypropan-2-yl (5Z,8Z,11Z,14Z)-eicosa-5,8,11,14-tetraenoate	53847-30-6

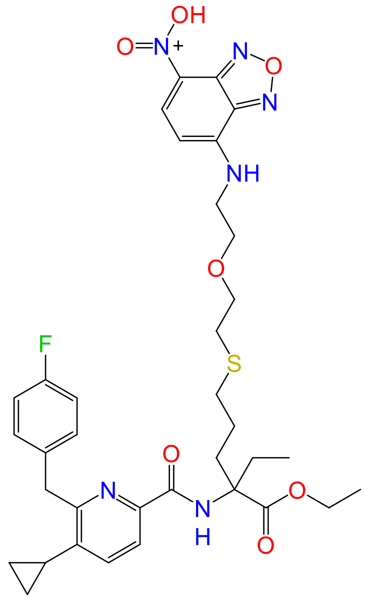
RO6435559		3-[(2-Chlorophenyl)methyl]-5-cyclopropyl-7-(4-ethylpiperazin-1-yl)-3H-[1,2,3]triazolo[4,5-d]pyrimidine	841215-25-6
RO6843766		Ethyl 2-{[6-(cyclopropylmethoxy)-5-(pyrrolidin-1-yl)pyridine-2-carbonyl]amino}-2-ethylbutanoate	1415897-32-3
RO6844112		Methyl N-{6-[(4-fluorophenyl)methyl]pyridine-2-carbonyl}-L-leucinate	Not existent

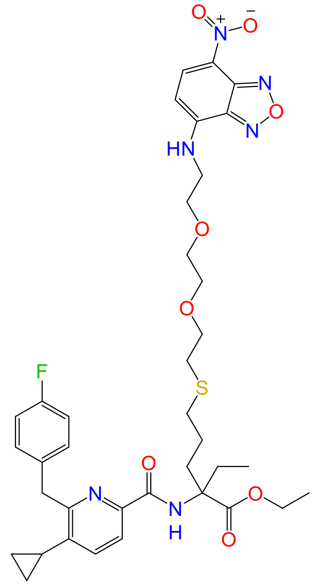
RO6844395		5-tert-Butyl-3-[(2-chlorophenyl)methyl]-7-(4-methylpiperazin-1-yl)-3H-[1,2,3]triazolo[4,5-d]pyrimidine	1433356-80-9
RO6850007		5-Cyclopropyl-4-(cyclopropylmethoxy)-N-[2,2-dimethyl-1-(1,3-thiazol-2-yl)propyl]pyridine-2-carboxamide	1613235-74-7
RO6853457		5-Cyclopropyl-N-[(2S)-3,3-dimethyl-1-(methylamino)-1-oxobutan-2-yl]-4-(2,2,2-trifluoroethoxy)pyridine-2-carboxamide	1613235-79-2

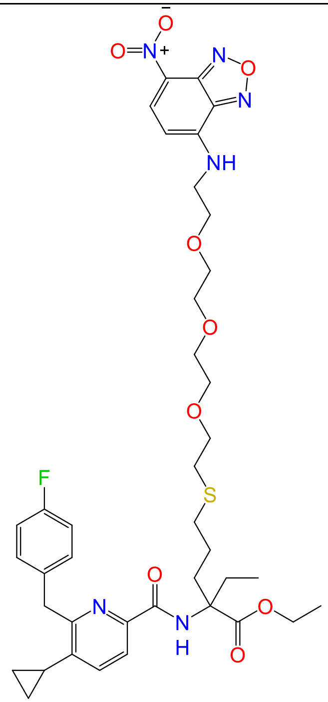
RO6853973		Ethyl N-{5-cyclopropyl-6-[(4-fluorophenyl)methyl]pyridine-2-carbonyl}-L-leucinate	1415900-27-4
RO6869094		3-[(2-Chlorophenyl)methyl]-N-cyclobutyl-7-(3,3-difluoropyrrolidin-1-yl)-N-methyl-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine	1672656-05-1
RO6871487		3-[(2-Chlorophenyl)methyl]-7-(3,3-difluoropyrrolidin-1-yl)-5-(phenylmethanesulfonyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidine	1672656-74-4

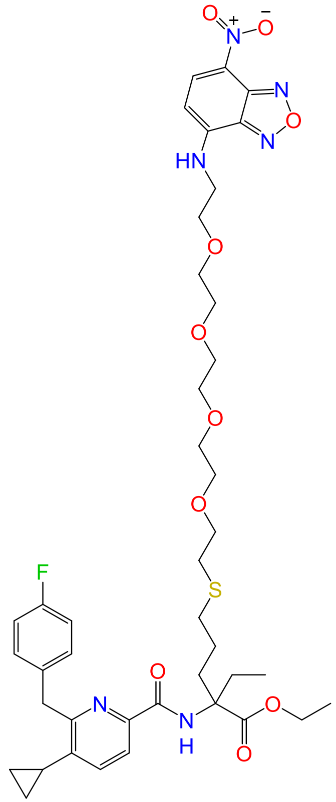
RO6878558		2-({3-[(2-Chlorophenyl)methyl]-7-(3,3-difluoropyrrolidin-1-yl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-yl}sulfanyl)ethan-1-ol	1672656-76-6
RO5135445		Methyl N-[6-(cyclobutylmethoxy)-5-(pyrrolidin-1-yl)pyrazine-2-carbonyl]-L-valinate	Not existent
RO6883666		5-(Butylsulfanyl)-3-[(2-chlorophenyl)methyl]-7-(3,3-difluoropyrrolidin-1-yl)-3H-[1,2,3]triazolo[4,5-d]pyrimidine	1672656-78-8

RO6892033		6-(3-tert-Butyl-1,2,4-oxadiazol-5-yl)-3-cyclopropyl-2-[(4-fluorophenyl)methyl]pyridine	Not existent
RO6926274		6-(5-tert-Butyl-1,2,4-oxadiazol-3-yl)-2-chloro-3-cyclopropyl-4-[(4-fluorophenyl)methoxy]pyridine	1629991-47-4
RO7032019		1-[6-(Cyclopropylmethoxy)-5-(3-fluoro-3-methylazetidin-1-yl)pyridine-2-carbonyl]-4,4-difluoro-L-prolinamide	1812888-93-9

FMP7234690		Ethyl N-{5-cyclopropyl-6-[(4-fluorophenyl)methyl]pyridine-2-carbonyl}-2-ethyl-5-[(2-{2-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]ethoxy}ethyl)sulfanyl]norvalinate	Not existent

FMP7234691		Ethyl N-{5-cyclopropyl-6-[(4-fluorophenyl)methyl]pyridine-2-carbonyl}-2-ethyl-5-{[2-(2-{2-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]ethoxy}ethoxy)ethyl]sulfanyl}norvalinate	Not existent

FMP7234694		Ethyl N-{5-cyclopropyl-6-[(4-fluorophenyl)methyl]pyridine-2-carbonyl}-2-ethyl-5-({2-[2-(2-{2-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]ethoxy}ethoxy)ethoxy]ethyl}sulfanyl)norvalinate	Not existent

FMP7234698		Ethyl N-{5-cyclopropyl-6-[(4-fluorophenyl)methyl]pyridine-2-carbonyl}-2-ethyl-5-({14-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]-3,6,9,12-tetraoxatetradecan-1-yl}sulfanyl)norvalinate	Not existent
FMP7234699		Ethyl N-{5-cyclopropyl-6-[(4-fluorophenyl)methyl]pyridine-2-carbonyl}-2-ethyl-5-({6-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]hexyl}sulfanyl)norvalinate	Not existent

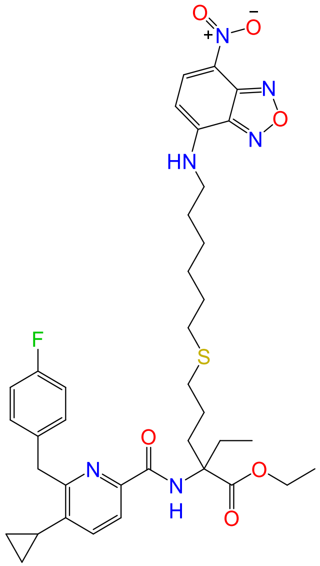
			

Table S2. In vitro pharmacology data for cannabinoid receptor ligands. CB2 selectivity calculated as $10^{pKi(CB2)-pKi(CB1)}$.

Compound	pK_i ± SE (hCB2)	pK_i ± SE (hCB1)	K_i (hCB1) / K_i (hCB2)	pK_i ± SE (mCB2)	cAMP pEC50 ± SE (hCB2)	cAMP E_{max} ± SE (hCB2)	cAMP pEC50 ± SE (hCB1)	cAMP E_{max} ± SE (hCB1)	cAMP pEC50 (hCB1) / cAMP pEC50 (hCB2)	cAMP pEC50 ± SE (mCB2)	cAMP E_{max} ± SE (mCB2)	β-arrestin pEC50 ± SE (hCB2)	β-arrestin E_{max} ± SE (hCB2)	β-arrestin pEC50 ± SE (hCB1)	β-arrestin E_{max} ± SE (hCB1)	β-arrestin pEC50 (hCB1) / β-arrestin pEC50 (hCB2)	β-arrestin pEC50 ± SE (mCB2)	β-arrestin E_{max} ± SE (mCB2)
SR144528	*7.88 ± 0.06*	*5.77 ± 0.09*	*129*	*10.7 ± 0.16*	*7.67 ± 0.18*	*-151 ± 10*	*< 5*	*n.a.*	*> 468*	*8.25 ± 0.29*	*-100*	*7.47 ± 0.27*	*-111 ± 3*	*4.97 ± 0.13*	*-82 ± 5*	*316*	< 4.5	-2
AM630	*7.39 ± 0.02*	*6.51 ± 0.25*	*8*	*7.66 ± 0.23*	*7.56 ± 0.05*	*-152 ± 13*	*< 5*	*28 ± 5*	*> 363*	*7.93 ± 0.3*	*-65*	*6.15 ± 0.08*	*-124 ± 6*	*5.56 ± 0.1*	*-120 ± 25*	*4*	< 4.5	-1
THC	*8.16 ± 0.17*	*8.48 ± 0.08*	*0.5*	*ND*	*ND*	*ND*	*ND*	*ND*	*ND*	*ND*	-	-	*31 ± 3§*	*6.29 ± 0.03*	*35 ± 3*	-	ND	ND

cannabinol	5.49 ± 0.01	6 ± 0.10	0.4	6.00 ± 0.05##	7.09 ± 0.07##	70	< 5	n.a.	> 123	7.59 ± 0.13	83	ND	ND	ND	ND	ND	ND	ND
(rac)-AM1241	8.39 ± 0.10	6.89 ± 0.31	32	7.73 ± 0.25	8.49± 0.08	67 ± 3	< 5	n.a.	3103	7.03 ± 0.26	-6	< 5	14 ± 2	< 5	6 ± 5	1	ND	ND
(*R*)-AM1241	8.44 ± 0.25	6.86 ± 0.46	38	7.59 ± 0.11	8.76 ± 0.18	65 ± 2	6.17 ± 0.12	54 ± 7	391	6.17 ± 0.23	-22	7.52 ± 0.43	29 ± 4	5.59 ± 0.13	26 ± 2	86	ND	ND
(*S*)-AM1241	7.02 ± 0.15	< 5	105	6.74 ± 0.2	7.40 ± 0.11	78 ± 1	< 5	16 ± 2	> 250	7.6 ± 0.3	35	6.54 ± 0.44	29 ± 8	< 5	2 ± 1	35	ND	ND
anandamide	6.91 ± 0.28	7.04 ± 0.28#	1	6.46 ± 0.18	5.93 ± 0.29	87± 7	< 5	39 ± 3	> 8	6.82 ± 0.51	48	6.21 ± 0.63	38 ± 3	-	36 ± 13§	-	ND	ND
HU210	9.78 ± 0.04	9.55 ± 0.06	2	9.27 ± 0.38	9.45 ± 0.27	94 ± 0.1	9.58 ± 0.24	104 ± 3	1	ND	ND	ND	ND	ND	ND	ND	ND	ND
nabilone	8.09 ± 0.04##	8.75 ± 0.08##	0.2	7.72 ± 0.04##	9.05 ± 0.24##	100	8.24 ± 0.11##	107	6	8.55 ± 0.07##	103	ND	ND	ND	ND	ND	ND	ND

HU308	7.44 ± 0.12	< 5	278	7.15 ± 0.21	8.53 ± 0.06	98 ± 1	< 5	18 ± 4	> 3388	8.43 ± 0.47	56	7.45 ± 0.07	57 ± 10	< 5	5.0 ± 1	282	6.47 ± 0.13	69 ± 3
WIN55212-2	8.57 ± 0.16	8.72 ± 0.24	1	7.28 ± 0.17	9.50 ± 0.09	98 ± 1	7.86 ± 0.23	107 ± 1	44	8.37 ± 0.23	97	7.93 ± 0.42	55 ± 5	6.74 ± 0.21	89 ± 2	15	< 5	-0.3
JWH133	7.18 ± 0.34	< 5	153	7.69 ± 0.23	8.38 ± 0.09	98 ± 1	< 5	37 ± 6	> 2399	7.75 ± 0.33	95	7.81 ± 0.22	62 ± 11	5.37 ± 0.05	40 ± 7	275	6.80 ± 0.17	63 ± 7
CP55940	8.44 ± 0.18	9.26 ± 0.12	0.2	9.22 ± 0.26	10.33 ± 0.09	98 ± 1	9.73 ± 0.10	100 ± 3	4	10.17 ± 0.3	100	8.39 ± 0.21	80 ± 5	7.96 ± 0.2	94 ± 2	3	8.02 ± 0.27	96 ± 1
2-AG	6.94 ± 0.43	7.15 ± 0.47#	1	7.53 ± 0.22	6.82 ± 0.05	94 ± 1	< 5	n.a.	> 67	7.15 ± 0.4	53	5.70 ± 0.21	80 ± 21	-	51 ± 21§	-	ND	ND
RO6435559	8.05 ± 0.09[##]	6.08 ± 0.09[##]	93	7.48 ± 0.09[##]	8.27 ± 0.10	77 ± 9	5.81 ± 0.28[##]	79	288	<5	-13	ND	ND	ND	ND	-	ND	ND
RO6843766	8.83 ± 0.05[##]	6.21 ± 0.03[##]	416	8.55 ± 0.03[##]	8.85 ± 0.15[##]	91	6.63 ± 0.16[##]	59	165	7.92 ± 0.05[##]	61	ND	ND	ND	ND	-	ND	ND

RO6844112	7.82 ± 0.06##	7.31 ± 0.08##	3	7.16 ± 0.03##	7.99 ± 0.02##	92	7.14 ± 0.07##	101	7	8.03 ± 0.16##	58	ND	ND	ND	ND	-	ND	ND
RO6844395	7.67 ± 0.04##	5.76 ± 0.05##	81	6.87 ± 0.05##	8.85 ± 0.22##	99	6.72 ± 0.17##	57	134	7.30 ± 0.05##	80	ND	ND	ND	ND	-	ND	ND
RO6850007	7.65 ± 0.21	5.83 ± 0.07##	66	9.21 ± 0.09##	8.49 ± 0.06##	63	<5	42	> 3090	8.23 ± 0.03##	-48	ND	ND	ND	ND	-	ND	ND
RO6853457	8.12 ± 0.22	5.99 ± 0.23	134	8.46 ± 0.27	8.81 ± 0.12	74 ± 2.1	6.18 ± 0.13##	75	426	8.42 ± 0.18	48 ± 8.3	ND	ND	5.47 ± 0.05##	3	>0.3	<4.5	-1
RO6853973	9.45 ± 0.16##	8.21 ± 0.09	17	9.17 ± 0.18	8.73 ± 0.12##	45	8.12 ± 0.05##	83	4	<5	23	ND	ND	ND	ND	-	ND	ND
RO6869094	7.71 ± 0.08##	5.96 ± 0.04##	56	8.39 ± 0.08##	8.09 ± 0.12##	48	6.01 ± 0.11##	60	120	<5	28	ND	ND	ND	ND	-	ND	ND
RO6871487	7.98 ± 0.11##	5.34 ± 0.10##	436	8.16 ± 0.08##	7.08 ± 0.13##	52	<5	9	> 120	<5	24	ND	ND	ND	ND	-	ND	ND

RO6878558	6.94 ± 0.04$^{\#\#}$	<5	> 87	6.69 ± 0.04$^{\#\#}$	8.13 ± 0.03$^{\#\#}$	87	<5	20	> 1348	8.40 ± 0.04$^{\#\#}$	92	ND	ND	ND	ND	-	ND	ND
RO5135445	8.97 ± 0.35	6.93 ± 0.08	109	7.06 ± 0.05$^{\#\#}$	8.63 ± 0.08	75 ± 9	6.36	74	186	7.89 ± 0.11$^{\#\#}$	64	ND	ND	ND	ND	-	ND	ND
RO6883666	7.41 ± 0.06$^{\#\#}$	6.00 ± 0.44$^{\#\#}$	25	7.77 ± 0.03$^{\#\#}$	8.16 ± 0.09$^{\#\#}$	67	<5	44	> 1445	<5	2	ND	ND	ND	ND	-	ND	ND
RO6892033	7.59 ± 0.06$^{\#\#}$	6.20 ± 0.06$^{\#\#}$	24	8.12 ± 0.14$^{\#\#}$	8.33 ± 0.10$^{\#\#}$	66	6.56 ± 0.08$^{\#\#}$	70	58	8.39 ± 0.32$^{\#\#}$	45	ND	ND	ND	ND	-	ND	ND
RO6926274	8.15 ± 0.12$^{\#\#}$	6.68 ± 0.05	29	7.40 ± 0.06$^{\#\#}$	8.32 ± 0.28$^{\#\#}$	38	7.14 ± 0.04$^{\#\#}$	73	15	6.29 ± 0.11	-160	ND	ND	ND	ND	-	ND	ND
RO7032019	7.38 ± 0.20$^{\#\#}$	<5	> 239	6.86 ± 0.07$^{\#\#}$	7.96 ± 0.08$^{\#\#}$	-92	<5	27	> 912	7.55 ± 0.09$^{\#\#}$	-87	ND	ND	ND	ND	-	ND	ND
FMP7234690	7.66 ± 0.09	6.38 ± 0.07	19	7.23 ± 0.08$^{\#\#}$	6.77 ± 0.19$^{\#\#}$	121	5.69 ± 0.35$^{\#\#}$	152	12	6.74 ± 0.20$^{\#\#}$	118	ND	ND	ND	ND	-	ND	ND

FMP7234691	7.65 ± 0.13	6.42 ± 0.14	16	7.14 ± 0.02[##]	8.33 ± 1.40	100 ± 1	6.22 ± 0.01	126 ± 5	128	6.99 ± 0.27[##]	118	ND	ND	ND	ND	-	ND	ND
FMP7234694	7.57 ± 0.13	6.34 ± 0.06	16	7.07 ± 0.05[##]	8.04 ± 0.28[##]	100	6.10 ± 0.14[##]	96	87	7.13 ± 0.16[##]	113	ND	ND	ND	ND	-	ND	ND
FMP7234698	7.42 ± 0.07	6.21 ± 0.06	16	6.93 ± 0.03[##]	7.69 ± 0.13[##]	102	5.95 ± 0.21[##]	110	54	6.72 ± 0.15[##]	117	ND	ND	ND	ND	-	ND	ND
FMP7234699	7.26 ± 0.03	5.97 ± 0.07	19	6.84 ± 0.05[##]	8.00 ± 0.14[##]	100	6.01 ± 0.10[##]	122	97	6.85 ± 0.16[##]	122	ND	ND	ND	ND	-	ND	ND

cAMP assays: the effect of 10 μM agonists is normalized to the effect of 10 μM CP55940, the potency of antagonists/inverse agonists is determined in presence of the EC_{80} of CP55940.
β-arrestin recruitment assays: the effect of 10 μM agonists is normalized to the effect of 10 μM CP55940, the potency of antagonists/inverse agonists is determined in presence of the EC_{80} of CP55940.
Negative values represent inhibition of the EC_{80} of CP55940 (> -100, indication of inverse agonism); n.a.: not active; ND = not determined. Effect at 10 μM.
[#] Mean ± SEM of 4 independent experiments.
[##] pKi values and ΔpKi errors were calculated from archived IC_{50} and standard error of the fit data using the Cheng-Prusoff equation for competitive binding and error propagation. pEC_{50} values and ΔpEC_{50} errors were calculated from archived EC_{50} and standard error of the fit data using error propagation.
§ E_{max} at 10 μM treatment, no plateau observed.
Italicized values described in Soethoudt *et al. Nat. Commun.* (2017) **8**: 13958.

Table S3. Calculated and measured physicochemical and early ADME properties with relevance for good *in vivo* performance of CB2 ligands. Green values from [1].

compound	MW (g/mol)	PSA[a] (Å^2)	HBD	K_{ow} clogP[b]	Log*D*[c] (at pH 7.4)	pK_a	kinetic solubility[d] (µg/mL)	PAMPA[e] P_{eff} (10^{-6} cm/s), %Acc./%Mem./%Don.	micros. CL human/mouse/rat (µL/min/kg)	hepat. CL human/mouse/rat (µL/min/million cells)	plasma protein binding: free fraction (%) human/mouse/rat	P-gp mediated efflux extraction ratio human/mouse
SR144528	*476.06*	*37.5*	*1*	*9.2*	*> 3*	*-*	*<0.2*	*0, 0 / 54 / 47*	*129 / 446 / 520*	*ND / ND / 8*	*<0.2 / ND / < 0.2*	*4.1 / 5.6*
AM630	*504.36*	*39.8*	*0*	*4.9*	*3.8*	*5.8 (B, calc.)*	*< 0.3*	*0.2, 0.4 / 64 / 35*	*82 / 468 / ND*	*18 / 101 / ND*	*<0.1 / 0.4 / ND*	*1.3 / 1.3*
THC	*314.47*	*22.2*	*1*	*7.6*	*ND*	*-*	*ND*	*ND*	*ND*	*ND*	*ND*	*ND*
cannabinol	*310.43*	*22.6*	*1*	*7.2*	*ND*	*9.8 (A, calc.)*	*ND*	*ND*	*ND*	*ND*	*ND*	*ND*
(*rac*)-AM1241	*503.33*	*62.5*	*0*	*5.7*	*3.66 ± 0.03*	*7.7 (B, calc.)*	*25 ± 2*	*1.86 ± 0.62, 3 / 56 / 41*	*111 / 254 / ND*	*ND*	*ND*	*ND*
(*R*)-AM1241	*503.33*	*62.6*	*0*	*5.7*	*3.66*	*7.8 (B)*	*12*	*1.22, 2 / 60 / 38*	*304 / 314 / ND*	*ND*	*ND*	*ND*
(*S*)-AM1241	*503.33*	*62.6*	*0*	*5.7*	*3.64*	*7.8 (B)*	*6*	*1.41, 2 / 64 / 34*	*152 / 640 / ND*	*34 / 251 / ND*	*0.5 / 1.2 / ND*	*2.7 / 1.4*
anandamide	*347.54*	*41.9*	*2*	*6.3*	*out of range*	*-*	*<1.1*	*0.26, 1 / 3 / 96*	*47 / 222 / ND*	*ND*	*ND*	*ND*
HU210	*386.57*	*38.0*	*2*	*8.0*	*prec.*	*-*	*<0.2*	*0.22, 0 / 76 / 23*	*25 / 33 / ND*	*ND*	*ND*	*ND*
nabilone	*372.55*	*37.9*	*1*	*7.1*	*ND*	*-*	*ND*	*ND*	*ND*	*ND*	*ND*	*ND*
HU308	*414.63*	*27.6*	*1*	*9.0*	*4.29*	*-*	*<0.8*	*2.53, 3 / 74 / 23*	*ND*	*8 / 5 / ND*	*ND*	*6.2 / 7.3*
WIN55912-2	*426.51*	*36.3*	*0*	*4.7*	*3.67 ± 0.03*	*5.5 (B, calc.)*	*<0.3*	*0.25 ± 0.22, 1 / 49 / 51*	*194 / 745 / ND*	*42 / 568 / ND*	*<0.3 / 1.0 / ND*	*1.5 / 1.4*
JWH133	*312.49*	*7.9*	*0*	*8.5*	*> 3 prec.*	*-*	*< 0.4*	*1.86, 2 / 62 / 36*	*38 / 63 / ND*	*6 / 10 / ND*	*<0.1 / <0.1 / <3.5*	*ND / 1.7*
CP55940	*376.58*	*49.9*	*3*	*7.5*	*ND*	*9.7 (A, calc.)*	*1.4*	*0, 0 / 47 / 53*	*80 / 745 / ND*	*ND*	*ND*	*ND*
2-AG	*378.55*	*51.3*	*2*	*6.7*	*ND*	*-*	*< 0.5*	*ND*	*13 / 12 / ND*	*ND*	*ND*	*ND*
RO6435559	397.91	55.0	0	4.0	ND	8.0 (B, calc.)	ND	ND	ND	ND	ND	ND
RO6843766	403.52	64.1	1	5.4	ND	2.4 (B, calc.)	ND	ND	ND	ND	ND	ND
RO6844112	358.41	55.6	1	4.5	ND	2.6 (B, calc.)	ND	ND	ND	ND	ND	ND
RO6844395	399.93	54.2	0	4.1	3.22	7.9 (B, calc.)	8	0.4, 1 / 45 / 54	27 / 491 / ND	ND	ND	ND
RO6850007	385.53	49.5	1	5.9	ND	11.1 (A, calc.), 3.7 and 2.7 (B, calc.)	ND	ND	ND	ND	ND	ND

RO6853457	387.40	64.9	2	3.2	3.89	2.6 (B, calc.)	92	3.9, 12 / 41 / 47	14 / 28 / 28	ND / 85 / ND	ND	ND
RO6853973	412.50	53.2	1	6.3	ND	2.2 (B, calc.)	ND	ND	ND	ND	ND	ND
RO6869094	433.89	52.7	0	5.6	ND	2.4 (B, calc.)	ND	ND	ND	ND	ND	ND
RO6871487	504.95	84.9	0	4.6	ND	-	ND	ND	ND	ND	ND	ND
RO6878558	426.88	69.8	1	3.4	ND	-	1	ND	56 / 174	ND	ND	ND
RO5135445	390.48	74.4	1	5.5	ND	3.6 (B, calc.)	ND	ND	ND	ND	ND	ND
RO6883666	438.93	53.0	0	5.9	ND	-	ND	ND	ND	ND	ND	ND
RO6892033	351.42	44.3	0	6.0	ND	< 2.0 (B)	1	0, 0 / 80 / 20	24 / 41 / ND	ND	ND	ND
RO6926274	401.87	49.7	0	6.2	ND	-	ND	ND	ND	ND	ND	ND
RO7032019	412.41	70.4	1	1.5	2.52	2.2 (B, calc.)	10	6.4, 12 / 43 / 45	10 / 10 / ND	ND	ND	ND
FMP7234690	708.80	151.3	2	9.0	ND	2.6 (B, calc.)	2	ND	59 / 46 / ND	ND	ND	ND
FMP7234691	752.85	160.0	2	8.8	2.84	2.6 and 2.0 (B, calc.)	9	ND	50 / 47 / ND	ND	ND	ND
FMP7234694	796.91	168.6	2	8.5	ND	2.6 and 2.0 (B, calc.)	14	0.7, 2 / 38 / 61	130 / 132 / ND	ND	ND	ND
FMP7234698	840.96	176.9	2	8.2	ND	2.6 and 2.0 (B, calc.)	6	0.7, 2 / 45 / 53	67 / 83 / ND	ND	ND	ND
FMP7234699	720.85	143.0	2	11.3	ND	2.6 (B, calc.)	14	0.5, 2 / 12 / 87	22 / 11 / ND	ND	ND	ND

MW – molecular weight; PSA – polar surface area; HBD – number of hydrogen-bond donors; B – basic; A – acidic; calc. – calculated; prec. – precipitated; micros. CL – microsomal clearance; hepat. CL – hepatocyte clearance; P-gp – P-glycoprotein; ND – not determined.

[a] Surface sum of all polar atoms in the molecule; [b] Calculated partition coefficient values (cLogP) from experimentally determined octanol/water partition coefficient values (K_{ow}); [c] Distribution coefficient values; [d]Solubility of the compound in aqueous buffer (pH 6.5) after lyophilization from DMSO superstock; [e] Parallel artificial membrane permeability assay (PAMPA) was used to determine membrane permeation coefficient values (P_{eff}), percentage of molecule that permeates into acceptor compartment, percentage of molecule found in membrane and percentage of molecule that stays in donor compartment.

Italicised values described in Soethoudt *et al. Nat. Commun.* (2017) **8**: 13958.

Table S4. Receptor and biosensor DNA amount used for transfection, optimized for the maximal ligand-induced response prior to ligand screen, given in nanograms of plasmid (pcDNA3.1 or pcDNA4) encoding for each biosensor component.

condition	receptor	β-arrestin-RlucII	GRK2	Gα	effector-RlucII	CAAX-rGFP	ssDNA
CB1, β-arrestin1	75	10	100	-	-	600	215
CB1, β-arrestin2	125	10	100	-	-	600	165
CB1, G_{i1}	25	-	-	100	10	500	365
CB1, G_{i2}	25	-	-	100	10	500	365
CB1, G_{i3}	25	-	-	100	10	600	265
CB1, G_{oA}	25	-	-	100	10	500	365
CB1, G_{oB}	25	-	-	100	10	500	365
CB1, G_{z}	25	-	-	100	10	600	265
CB1, G_{12}	25	-	-	100	10	500	365
CB1, G_{13}	25	-	-	100	5	500	370
CB1, G15	25	-	-	100	10	500	365
CB2, β-arrestin1	75	25	100	-	-	600	200
CB2, β-arrestin2	125	10	100	-	-	600	165
CB2, G_{i1}	25	-	-	150	10	400	415
CB2, G_{i2}	10	-	-	150	10	400	430
CB2, G_{i3}	10	-	-	150	10	600	230
CB2, G_{oA}	25	-	-	150	10	600	215
CB2, G_{oB}	25	-	-	150	10	600	215

Table S5. Receptor and biosensor DNA amount used for transfection, optimized for the maximal ligand-induced response prior to ligand screen, given in nanograms of plasmid (pcDNA3.1 or pcDNA4) encoding for each biosensor component.

condition	receptor	β-arrestin-RlucII	GRK2	FYVE-rGFP	ssDNA
V2R, β-arrestin1	5	10	-	600	385
V2R, β-arrestin2	5	10	-	600	385
CB1, β-arrestin1	75	10	100	600	215
CB1, β-arrestin2	125	10	100	600	165
CB2, β-arrestin1	75	25	100	600	200
CB2, β-arrestin2	125	10	100	600	165

Table S6. Receptor and biosensor DNA amount used for transfection of Gα–Gβγ dissociation-based G protein biosensor, given in nanograms of plasmid (pcDNA3.1 or pcDNA4) encoding for each biosensor component.

condition	**receptor**	**Gα-RlucII**	**$G\beta_1$**	**$G\gamma_2$-GFP10**	**ssDNA**
CB1, G_s	200	100	100	400	200
CB2, G_s	100	400	100	400	0

Table S7. Maximal ligand-induced response (E_{max}) indicates which pathways are activated by CB1 and CB2. Mean and standard error or mean (SE) from four technical replicates are shown.

pathway	CB1		CB2	
	mean	**SE**	**mean**	**SE**
G_{i1}	0.173	0.014	0.264	0.034
G_{i2}	0.357	0.092	0.613	0.023
G_{i3}	0.158	0.018	0.198	0.026
G_{oA}	0.296	0.019	0.220	0.053
G_{oB}	0.429	0.058	0.898	0.068
G_z	0.299	0.061	0.191	0.119
G_q	0.025	0.015	0.010	0.008
G_{11}	0.015	0.010	0.007	0.009
G_{14}	-0.006	0.010	0.005	0.022
G_{15}	0.214	0.012	-0.004	0.015
G_{12}	0.125	0.021	0.011	0.012
G_{13}	0.150	0.015	0.008	0.013
G_s	-0.006	0.005	0.010	0.009
β-arrestin1	0.044	0.015	0.110	0.031
β-arrestin2	0.261	0.013	0.300	0.027

Table S8. Maximal ligand-induced response (E_{max}) and negative logarithm of half-maximal response concentration (pEC50) values extracted from CB1 ligand screen data, reported as mean of three biological replicates and the corresponding standard errors (SE).

pathway		HU210	WIN55212-2	CP55940	nabilone	THC	cannabinol	anandamide	2-AG
G_{i1}	pEC50	9.419	8.413	9.172	8.282	8.595	8.387	6.978	6.822
	SE (pEC50)	0.121	0.086	0.119	0.108	0.120	0.231	0.096	0.194
	E_{max}	0.358	0.647	0.326	0.321	0.532	0.244	0.164	0.317
	SE (E_{max})	0.029	0.038	0.026	0.023	0.043	0.038	0.011	0.042
G_{i2}	pEC50	9.413	8.115	9.604	8.982	8.607	7.807	7.421	7.168
	SE (pEC50)	0.121	0.086	0.119	0.108	0.120	0.231	0.096	0.194
	E_{max}	0.647	0.618	0.617	0.574	0.350	0.240	0.551	0.551
	SE (E_{max})	0.029	0.038	0.026	0.023	0.043	0.038	0.011	0.042
G_{i3}	pEC50	9.172	7.484	9.426	9.102	8.466	7.885	7.364	6.830
	SE (pEC50)	0.119	0.114	0.108	0.133	0.166	0.333	0.107	0.096
	E_{max}	0.326	0.348	0.334	0.292	0.180	0.080	0.243	0.296
	SE (E_{max})	0.026	0.028	0.024	0.027	0.020	0.018	0.018	0.020
G_{oA}	pEC50	9.282	8.090	9.847	9.246	8.731	7.834	7.588	6.828
	SE (pEC50)	0.108	0.101	0.126	0.192	0.196	0.322	0.128	0.198
	E_{max}	0.321	0.419	0.440	0.408	0.284	0.131	0.365	0.384
	SE (E_{max})	0.023	0.029	0.038	0.056	0.038	0.029	0.032	0.052
G_{oB}	pEC50	9.595	8.189	9.612	9.348	8.524	7.591	7.694	6.978
	SE (pEC50)	0.120	0.075	0.114	0.142	0.230	0.188	0.099	0.123
	E_{max}	0.532	0.713	0.665	0.625	0.379	0.303	0.525	0.621
	SE (E_{max})	0.043	0.036	0.052	0.064	0.059	0.039	0.035	0.053
G_z	pEC50	9.387	8.321	9.857	9.016	8.470	6.940	7.712	7.000
	SE (pEC50)	0.231	0.142	0.173	0.277	0.263	0.405	0.304	0.186
	E_{max}	0.244	0.399	0.316	0.251	0.189	0.188	0.157	0.291
	SE (E_{max})	0.038	0.039	0.038	0.049	0.034	0.057	0.033	0.038
G_{12}	pEC50	8.978	7.413	8.932	8.442	7.961	8.843	6.790	6.069
	SE (pEC50)	0.096	0.071	0.090	0.112	0.231	0.525	0.101	0.051
	E_{max}	0.164	0.291	0.230	0.196	0.055	0.025	0.134	0.270
	SE (E_{max})	0.011	0.014	0.014	0.015	0.009	0.009	0.009	0.010
G_{13}	pEC50	8.750	7.497	8.866	8.310	7.923	7.300	7.047	6.148
	SE (pEC50)	0.053	0.055	0.058	0.080	0.180	0.155	0.072	0.045
	E_{max}	0.300	0.385	0.345	0.341	0.151	0.121	0.276	0.416
	SE (E_{max})	0.011	0.015	0.014	0.018	0.018	0.013	0.014	0.013
G_{15}	pEC50	8.913	7.285	9.043	8.576	8.572	6.116	6.921	6.083
	SE (pEC50)	0.247	0.111	0.173	0.120	0.523	0.464	0.191	0.088
	E_{max}	0.140	0.316	0.257	0.218	0.048	-0.117	0.143	0.375

	SE (E_{max})	0.024	0.025	0.030	0.018	0.017	0.051	0.019	0.024
β-arrestin1	pEC50	8.313	7.044	8.886	8.192	7.660	0.000	6.826	4.867
	SE (pEC50)	0.131	0.125	0.155	0.122	0.428	0.000	0.294	0.101
	E_{max}	0.074	0.117	0.058	0.070	0.028	0.000	0.045	0.214
	SE (E_{max})	0.007	0.011	0.006	0.006	0.008	0.000	0.009	0.018
β-arrestin2	pEC50	8.353	7.137	8.680	8.102	7.927	6.713	6.646	5.321
	SE (pEC50)	0.038	0.041	0.038	0.047	0.108	0.273	0.063	0.027
	E_{max}	0.318	0.445	0.271	0.317	0.085	0.040	0.214	0.587
	SE (E_{max})	0.009	0.013	0.007	0.010	0.006	0.009	0.009	0.012

Table S9. Maximal ligand-induced response (E_{max}) and negative logarithm of half-maximal response concentration (pEC50) values extracted from CB2 ligand screen data, reported as mean of three independent experiments and the corresponding standard errors (SE).

ligand		G_{i1}	G_{i2}	G_{i3}	G_{oA}	G_{oB}	β-arrestin1	β-arrestin2
JWH133	pEC50	8.791	7.811	8.298	7.979	8.535	8.237	7.973
	SE (pEC50)	0.122	0.108	0.078	0.082	0.059	0.151	0.123
	E_{max}	0.294	0.692	0.358	0.416	0.862	0.101	0.229
	SE (E_{max})	0.025	0.051	0.019	0.023	0.035	0.010	0.019
HU308	pEC50	8.167	8.008	7.793	7.490	7.914	7.560	7.613
	SE (pEC50)	0.075	0.073	0.085	0.175	0.078	0.267	0.155
	E_{max}	0.372	0.899	0.431	0.583	0.974	0.066	0.194
	SE (E_{max})	0.026	0.064	0.041	0.137	0.078	0.012	0.020
(*rac*)-AM1241	pEC50	8.358	7.994	7.946	7.980	8.171	8.031	8.063
	SE (pEC50)	0.193	0.160	0.171	0.212	0.112	0.376	0.313
	E_{max}	0.193	0.375	0.130	0.120	0.437	0.032	0.039
	SE (E_{max})	0.025	0.041	0.015	0.017	0.033	0.008	0.008
AM630	pEC50	8.198	8.023	8.369	7.643	8.396	0.000	7.771
	SE (pEC50)	0.116	0.091	0.182	0.267	0.107	0.000	0.333
	E_{max}	-0.211	-0.381	-0.067	-0.096	-0.315	0.000	-0.037
	SE (E_{max})	0.017	0.024	0.008	0.018	0.023	0.000	0.008
(*R*)-AM1241	pEC50	8.299	8.227	8.339	8.555	8.120	0.000	8.399
	SE (pEC50)	0.164	0.128	0.161	0.219	0.095	0.000	0.287
	E_{max}	0.212	0.364	0.138	0.105	0.409	0.000	0.056
	SE (E_{max})	0.024	0.032	0.015	0.014	0.026	0.000	0.011
(*S*)-AM1241	pEC50	7.434	7.308	7.338	6.975	7.329	7.323	6.734
	SE (pEC50)	0.143	0.086	0.098	0.119	0.079	0.347	0.131
	E_{max}	0.273	0.582	0.285	0.275	0.627	0.047	0.155
	SE (E_{max})	0.027	0.035	0.020	0.024	0.035	0.012	0.015
HU210	pEC50	9.414	9.594	9.273	9.138	9.591	9.309	9.361
	SE (pEC50)	0.136	0.077	0.136	0.082	0.071	0.223	0.150
	E_{max}	0.321	0.670	0.327	0.347	0.716	0.085	0.152
	SE (E_{max})	0.030	0.035	0.030	0.019	0.035	0.012	0.016
WIN55212-2	pEC50	9.409	9.520	9.326	9.095	9.271	9.284	9.468
	SE (pEC50)	0.047	0.045	0.042	0.064	0.049	0.197	0.132
	E_{max}	0.404	0.703	0.376	0.388	0.830	0.081	0.196
	SE (E_{max})	0.013	0.022	0.011	0.018	0.029	0.011	0.019
CP55940	pEC50	10.010	9.972	9.985	9.574	9.908	9.393	9.383
	SE (pEC50)	0.137	0.087	0.096	0.099	0.075	0.189	0.125
	E_{max}	0.244	0.640	0.345	0.394	0.813	0.102	0.269
	SE (E_{max})	0.023	0.039	0.023	0.027	0.042	0.013	0.022
nabilone	pEC50	8.885	9.165	8.977	8.297	8.737	8.640	8.658
	SE (pEC50)	0.186	0.106	0.123	0.068	0.085	0.267	0.151
	E_{max}	0.319	0.511	0.322	0.396	0.759	0.087	0.193
	SE (E_{max})	0.041	0.038	0.027	0.018	0.044	0.016	0.020
THC	pEC50	8.123	7.886	7.791	8.597	8.116	0.000	8.458
	SE (pEC50)	0.249	0.172	0.216	0.419	0.142	0.000	0.577
	E_{max}	0.110	0.231	0.104	0.070	0.259	0.000	0.028
	SE (E_{max})	0.018	0.027	0.015	0.020	0.025	0.000	0.011

cannabinol	pEC50	7.820	7.506	7.356	8.350	7.662	0.000	6.664
	SE (pEC50)	0.246	0.165	0.122	0.220	0.147	0.000	0.480
	E_{max}	0.164	0.307	0.152	0.140	0.338	0.000	0.033
	SE (E_{max})	0.028	0.035	0.013	0.021	0.034	0.000	0.012
anandamide	pEC50	7.415	7.173	7.165	7.095	7.563	5.448	6.509
	SE (pEC50)	0.126	0.086	0.092	0.140	0.105	0.175	0.224
	E_{max}	0.266	0.520	0.220	0.207	0.587	0.109	0.094
	SE (E_{max})	0.023	0.030	0.014	0.020	0.042	0.016	0.015
2-AG	pEC50	7.027	6.827	6.742	6.797	7.140	5.997	5.979
	SE (pEC50)	0.156	0.088	0.097	0.115	0.078	0.121	0.090
	E_{max}	0.331	0.659	0.343	0.325	0.711	0.141	0.316
	SE (E_{max})	0.037	0.042	0.024	0.026	0.040	0.012	0.021
SR144528	pEC50	8.624	8.353	8.825	9.318	9.004	8.523	9.173
	SE (pEC50)	0.099	0.099	0.152	0.175	0.114	0.288	0.168
	E_{max}	-0.264	-0.410	-0.112	-0.084	-0.355	-0.033	-0.060
	SE (E_{max})	0.018	0.029	0.012	0.010	0.028	0.007	0.007
RO6843766	pEC50	9.341	9.096	9.127	9.110	9.314	9.967	9.557
	SE (pEC50)	0.181	0.101	0.115	0.152	0.079	0.443	0.234
	E_{max}	0.226	0.422	0.213	0.177	0.504	0.028	0.068
	SE (E_{max})	0.028	0.029	0.017	0.018	0.027	0.009	0.011
RO6853457	pEC50	8.431	8.535	8.344	8.290	8.045	7.960	7.655
	SE (pEC50)	0.182	0.087	0.161	0.212	0.096	0.471	0.251
	E_{max}	0.193	0.392	0.114	0.127	0.389	0.033	0.081
	SE (E_{max})	0.025	0.024	0.013	0.019	0.027	0.011	0.016
RO7032019	pEC50	8.588	8.561	8.103	8.137	8.423	8.130	8.226
	SE (pEC50)	0.299	0.145	0.149	0.159	0.100	0.368	0.213
	E_{max}	0.077	0.416	0.184	0.210	0.606	0.031	0.064
	SE (E_{max})	0.016	0.042	0.020	0.024	0.042	0.008	0.010
RO6871487	pEC50	8.016	8.085	8.540	8.430	8.160	0.000	8.037
	SE (pEC50)	0.193	0.105	0.216	0.193	0.156	0.000	0.674
	E_{max}	0.144	0.313	0.074	0.106	0.249	0.000	0.026
	SE (E_{max})	0.020	0.024	0.011	0.014	0.028	0.000	0.013
RO6878558	pEC50	7.945	7.986	7.893	8.028	7.824	8.512	7.624
	SE (pEC50)	0.152	0.123	0.192	0.169	0.079	0.370	0.487
	E_{max}	0.230	0.419	0.144	0.154	0.555	0.029	0.054
	SE (E_{max})	0.026	0.038	0.021	0.019	0.033	0.007	0.021
RO6883666	pEC50	8.021	7.652	7.986	8.613	7.903	0.000	0.000
	SE (pEC50)	0.148	0.146	0.417	0.259	0.158	0.000	0.000
	E_{max}	0.165	0.351	0.060	0.100	0.305	0.000	0.000
	SE (E_{max})	0.018	0.041	0.018	0.018	0.036	0.000	0.000
RO6853973	pEC50	9.052	9.450	9.296	9.017	9.329	0.000	0.000
	SE (pEC50)	0.183	0.163	0.394	0.262	0.215	0.000	0.000
	E_{max}	0.141	0.181	0.049	0.076	0.167	0.000	0.000
	SE (E_{max})	0.018	0.020	0.013	0.014	0.024	0.000	0.000
RO6850007	pEC50	8.267	8.237	7.925	8.319	8.709	8.371	8.806

	SE (pEC50)	0.201	0.188	0.321	0.322	0.277	0.747	0.553
	E_{max}	0.110	0.179	0.070	0.119	0.191	0.034	0.045
	SE (E_{max})	0.016	0.024	0.017	0.027	0.036	0.018	0.017
RO6844395	pEC50	7.855	7.499	7.994	7.607	7.665	0.000	7.671
	SE (pEC50)	0.137	0.106	0.127	0.167	0.103	0.000	0.274
	E_{max}	0.205	0.537	0.167	0.274	0.637	0.000	0.077
	SE (E_{max})	0.021	0.046	0.016	0.036	0.051	0.000	0.016
RO6844112	pEC50	8.632	8.496	8.160	8.159	8.497	7.714	8.242
	SE (pEC50)	0.109	0.083	0.121	0.165	0.080	0.189	0.269
	E_{max}	0.273	0.554	0.223	0.208	0.628	0.056	0.090
	SE (E_{max})	0.021	0.032	0.019	0.025	0.035	0.008	0.017
RO5135445	pEC50	8.748	9.121	8.563	8.718	8.504	8.438	9.551
	SE (pEC50)	0.164	0.108	0.161	0.218	0.096	0.431	0.659
	E_{max}	0.182	0.345	0.119	0.153	0.470	0.037	0.041
	SE (E_{max})	0.020	0.025	0.013	0.023	0.031	0.011	0.019
RO6926274	pEC50	8.574	9.040	8.202	8.250	8.765	0.000	0.000
	SE (pEC50)	0.436	0.216	0.239	0.330	0.417	0.000	0.000
	E_{max}	0.086	0.178	0.078	0.105	0.108	0.000	0.000
	SE (E_{max})	0.026	0.026	0.015	0.025	0.031	0.000	0.000
RO6892033	pEC50	8.536	8.599	8.856	8.018	8.328	8.566	0.000
	SE (pEC50)	0.219	0.114	0.225	0.225	0.148	0.161	0.000
	E_{max}	0.135	0.301	0.095	0.173	0.305	0.050	0.000
	SE (E_{max})	0.020	0.024	0.015	0.029	0.032	0.006	0.000
RO6435559	pEC50	7.984	8.154	7.941	7.998	7.794	8.518	8.131
	SE (pEC50)	0.152	0.131	0.246	0.192	0.110	0.235	0.326
	E_{max}	0.202	0.359	0.125	0.217	0.415	0.028	0.024
	SE (E_{max})	0.023	0.034	0.023	0.031	0.035	0.005	0.006
RO6869094	pEC50	8.214	8.341	7.645	0.000	8.321	9.084	8.016
	SE (pEC50)	0.340	0.198	0.561	0.000	0.217	0.251	0.310
	E_{max}	0.070	0.158	0.055	0.000	0.148	0.028	0.027
	SE (E_{max})	0.017	0.022	0.024	0.000	0.023	0.005	0.006
FMP7234690	pEC50	7.991	8.358	7.571	7.302	8.018	8.536	8.042
	SE (pEC50)	0.133	0.097	0.121	0.207	0.088	0.604	0.297
	E_{max}	0.222	0.438	0.259	0.240	0.606	0.033	0.094
	SE (E_{max})	0.022	0.030	0.025	0.043	0.039	0.014	0.021
FMP7234691	pEC50	8.148	8.416	8.173	7.954	7.997	8.981	8.224
	SE (pEC50)	0.132	0.075	0.095	0.161	0.076	0.503	0.181
	E_{max}	0.271	0.561	0.249	0.309	0.669	0.046	0.156
	SE (E_{max})	0.026	0.030	0.017	0.037	0.038	0.016	0.020
FMP7234694	pEC50	7.846	8.210	7.982	8.199	8.243	8.120	8.109
	SE (pEC50)	0.124	0.062	0.103	0.144	0.084	0.616	0.108
	E_{max}	0.251	0.585	0.267	0.316	0.601	0.032	0.161
	SE (E_{max})	0.023	0.026	0.020	0.033	0.036	0.014	0.013
FMP7234698	pEC50	7.781	8.041	8.165	8.429	8.449	8.851	7.858
	SE (pEC50)	0.115	0.113	0.161	0.125	0.080	0.207	0.096

	E_{max}	0.258	0.519	0.247	0.354	0.600	0.067	0.188
	SE (E_{max})	0.023	0.043	0.029	0.031	0.034	0.010	0.014
FMP7234699	pEC50	7.933	7.960	7.886	8.330	7.866	8.094	8.058
	SE (pEC50)	0.141	0.126	0.136	0.158	0.093	0.175	0.153
	E_{max}	0.222	0.590	0.224	0.337	0.671	0.072	0.144
	SE (E_{max})	0.023	0.055	0.023	0.038	0.047	0.009	0.016

Table S10. Concentration-response CB1-mediated signaling by anandamide. Mean and standard error of mean (SE) from three biological replicates are shown.

$\log\left(\frac{[\text{ligand}]}{\text{mol L}^{-1}}\right)$	**G_{i2}**		**G_{oB}**		**G_z**		**G_{12}**		**G_{13}**		**G_{15}**		**β-arrestin1**		**β-arrestin2**	
	mean	SE	mean	SE	mean	SE	mean	SE	mean	SE	mean	SE	mean	SE	mean	SE
-10	0.037	0.074	0.032	0.057	0.055	0.061	0.008	0.020	-0.045	0.025	0.038	0.054	0.037	0.050	0.015	0.014
-9.5	-0.076	0.047	0.017	0.034	0.043	0.089	-0.011	0.022	0.003	0.030	0.037	0.045	-0.037	0.069	-0.001	0.013
-9	0.031	0.054	-0.003	0.080	-0.007	0.076	0.019	0.033	0.012	0.035	-0.015	0.056	0.010	0.064	0.007	0.010
-8.5	0.120	0.051	0.127	0.042	-0.033	0.064	-0.018	0.014	0.051	0.040	-0.045	0.054	0.030	0.087	0.011	0.015
-8	0.184	0.058	0.205	0.047	0.118	0.059	0.043	0.024	0.086	0.038	0.014	0.075	-0.005	0.050	0.012	0.013
-7.5	0.413	0.060	0.426	0.042	0.256	0.072	0.058	0.028	0.196	0.038	0.114	0.057	0.061	0.057	0.042	0.013
-7	0.626	0.048	0.685	0.030	0.420	0.059	0.211	0.034	0.379	0.049	0.220	0.036	0.174	0.088	0.140	0.015
-6.5	0.792	0.087	0.751	0.023	0.370	0.060	0.280	0.030	0.536	0.040	0.340	0.044	0.207	0.083	0.293	0.009
-6	0.888	0.085	0.685	0.051	0.341	0.066	0.387	0.022	0.646	0.036	0.350	0.056	0.413	0.089	0.399	0.024
-5.5	0.831	0.076	0.698	0.037	0.352	0.096	0.424	0.026	0.704	0.033	0.378	0.061	0.362	0.082	0.443	0.033
-5	0.827	0.072	0.712	0.047	0.432	0.085	0.487	0.059	0.702	0.027	0.484	0.083	0.378	0.095	0.459	0.029
-4.5	0.989	0.125	0.739	0.057	0.369	0.136	0.448	0.033	0.733	0.018	0.499	0.054	0.345	0.079	0.483	0.031

Table S11. Concentration-response CB1-mediated signaling by 2-AG. Mean and standard error of mean (SE) from three biological replicates are shown.

$\log\left(\frac{[\text{ligand}]}{\text{mol L}^{-1}}\right)$	**G_{i2}**		**G_{oB}**		**G_z**		**G_{12}**		**G_{13}**		**G_{15}**		**β-arrestin1**		**β-arrestin2**	
	mean	SE	mean	SE	mean	SE	mean	SE	mean	SE	mean	SE	mean	SE	mean	SE
-9.3	-0.082	0.059	-0.031	0.048	0.008	0.088	-0.004	0.032	-0.021	0.026	0.039	0.050	-0.099	0.055	-0.007	0.010
-8.8	0.068	0.050	0.034	0.053	-0.040	0.064	0.013	0.018	-0.032	0.021	-0.124	0.070	-0.041	0.091	-0.010	0.007
-8.3	0.063	0.070	0.057	0.056	0.059	0.045	0.002	0.028	0.004	0.025	-0.048	0.060	-0.039	0.083	-0.016	0.011
-7.8	0.241	0.079	0.123	0.062	0.142	0.072	0.018	0.024	0.052	0.023	0.037	0.051	-0.044	0.081	-0.020	0.015
-7.3	0.374	0.081	0.260	0.074	0.231	0.113	0.051	0.024	0.113	0.029	0.161	0.073	0.003	0.056	0.005	0.010
-6.8	0.586	0.063	0.538	0.075	0.439	0.070	0.133	0.027	0.177	0.024	0.250	0.067	0.055	0.047	0.039	0.026
-6.3	0.760	0.083	0.718	0.083	0.629	0.116	0.353	0.039	0.477	0.038	0.474	0.035	0.154	0.070	0.207	0.029
-5.8	0.859	0.112	0.806	0.078	0.610	0.083	0.593	0.032	0.737	0.039	0.759	0.058	0.330	0.071	0.337	0.019
-5.3	0.890	0.085	0.861	0.080	0.735	0.097	0.809	0.039	0.896	0.031	0.917	0.048	0.502	0.060	0.680	0.018
-4.8	0.899	0.091	0.898	0.073	0.770	0.096	0.862	0.018	1.011	0.029	1.054	0.054	1.027	0.155	0.960	0.018
-4.3	0.904	0.123	0.814	0.091	0.653	0.103	0.917	0.036	1.126	0.023	1.321	0.081	1.184	0.103	1.187	0.023
-3.8	0.888	0.170	0.923	0.123	0.801	0.132	-	-	-	-	-	-	1.864	0.144	1.332	0.017

Table S12. Concentration-response CB2-mediated signaling by anandamide. Mean and standard error or mean (SE) from three independent experiments are shown.

$\log\left(\frac{[\text{ligand}]}{\text{mol L}^{-1}}\right)$	G_{i2}		G_{oB}		β-arrestin1		β-arrestin2	
	mean	SE	mean	SE	mean	SE	mean	SE
-10	0.027	0.033	0.037	0.033	-0.125	0.082	-0.047	0.051
-9.5	0.000	0.038	-0.022	0.042	-0.021	0.097	0.071	0.079
-9	-0.013	0.048	0.019	0.054	0.014	0.139	0.105	0.088
-8.5	0.044	0.027	0.040	0.041	-0.015	0.089	0.009	0.055
-8	0.063	0.027	0.241	0.051	-0.097	0.088	-0.054	0.044
-7.5	0.262	0.037	0.379	0.076	0.012	0.113	-0.028	0.047
-7	0.479	0.039	0.533	0.053	0.231	0.109	0.107	0.051
-6.5	0.559	0.056	0.607	0.049	0.175	0.096	0.238	0.061
-6	0.635	0.041	0.685	0.060	0.327	0.097	0.397	0.050
-5.5	0.712	0.037	0.727	0.050	0.607	0.101	0.502	0.102
-5	0.760	0.045	0.713	0.037	0.909	0.154	0.473	0.095
-4.5	0.792	0.065	0.722	0.041	1.259	0.181	0.391	0.066

Table S13. Concentration-response CB2-mediated signaling by 2-AG. Mean and standard error or mean (SE) from three independent experiments are shown.

$\log\left(\frac{[\text{ligand}]}{\text{mol L}^{-1}}\right)$	G_{i2}		G_{oB}		β-arrestin1		β-arrestin2	
	mean	SE	mean	SE	mean	SE	mean	SE
-9.3	-0.016	0.030	-0.052	0.036	-0.248	0.117	-0.053	0.044
-8.8	-0.014	0.034	0.034	0.040	-0.150	0.083	0.020	0.032
-8.3	0.024	0.041	0.107	0.037	0.012	0.082	0.029	0.038
-7.8	0.115	0.033	0.148	0.050	0.179	0.100	0.043	0.047
-7.3	0.297	0.022	0.360	0.048	0.227	0.086	0.061	0.062
-6.8	0.461	0.045	0.546	0.051	0.397	0.123	0.196	0.085
-6.3	0.704	0.059	0.767	0.030	0.630	0.133	0.579	0.125
-5.8	0.810	0.078	0.852	0.029	0.884	0.194	0.952	0.128
-5.3	0.838	0.085	0.894	0.037	1.395	0.156	1.250	0.126
-4.8	1.061	0.038	0.818	0.056	1.783	0.138	1.667	0.079
-4.3	0.980	0.063	0.791	0.036	1.643	0.096	1.510	0.116
-3.8	-	-	-	-	1.548	0.236	1.622	0.192

Table S14. Calculation of CB1 relative effectiveness (RE = $10^{\Delta \log R}$) as described in van der Westhuizen *et al.*, using WIN55212-2 as a reference ligand. NC = not converged, ND = not determined, IA = inverse agonist. ΔlogR = logR(ligand) - logR(reference).

pathway		WIN55,212-2	HU210	CP55940	nabilone	anandamide	2-AG	THC	cannabinol
G_{i1}	logR	8.414	9.162	8.874	7.978	6.382	6.512	8.512	7.965
	SE (logR)	0.064	0.108	0.120	0.121	0.239	0.123	0.073	0.159
	ΔlogR	0.000	0.748	0.460	-0.436	-2.032	-1.902	0.098	-0.449
	SE (ΔlogR)	0.091	0.126	0.136	0.137	0.248	0.138	0.097	0.171
	RE	1.000	5.598	2.884	0.366	0.009	0.013	1.253	0.356
G_{i2}	logR	8.094	9.414	9.583	8.931	7.353	7.099	8.519	7.378
	SE (logR)	0.085	0.086	0.084	0.090	0.095	0.094	0.143	0.220
	ΔlogR	0.000	1.320	1.489	0.837	-0.741	-0.995	0.425	-0.716
	SE (ΔlogR)	0.121	0.121	0.120	0.124	0.127	0.127	0.166	0.236
	RE	1.000	20.893	30.832	6.871	0.182	0.101	2.661	0.192
G_{i3}	logR	7.484	9.143	9.408	9.026	7.207	6.759	8.161	7.243
	SE (logR)	0.086	0.082	0.079	0.089	0.108	0.110	0.142	0.332
	ΔlogR	0.000	1.659	1.924	1.542	-0.277	-0.725	0.677	-0.241
	SE (ΔlogR)	0.122	0.119	0.117	0.124	0.138	0.139	0.166	0.343
	RE	1.000	45.604	83.946	34.834	0.528	0.188	4.753	0.574
G_{oA}	logR	8.068	9.145	9.847	9.213	7.506	6.768	8.603	7.308
	SE (logR)	0.105	0.135	0.102	0.104	0.118	0.113	0.147	0.334
	ΔlogR	0.000	1.077	1.779	1.145	-0.562	-1.300	0.535	-0.760
	SE (ΔlogR)	0.149	0.171	0.147	0.148	0.158	0.154	0.181	0.351
	RE	1.000	11.940	60.117	13.964	0.274	0.050	3.428	0.174
G_{oB}	logR	8.189	9.470	9.581	9.291	7.562	6.919	8.613	7.221
	SE (logR)	0.078	0.097	0.078	0.082	0.098	0.084	0.126	0.176
	ΔlogR	0.000	1.281	1.392	1.102	-0.627	-1.270	0.424	-0.968
	SE (ΔlogR)	0.111	0.125	0.111	0.113	0.126	0.115	0.148	0.193
	RE	1.000	19.099	24.660	12.647	0.236	0.054	2.655	0.108
G_z	logR	8.322	9.174	9.753	8.816	7.304	6.863	8.032	6.613
	SE (logR)	0.118	0.181	0.139	0.173	0.278	0.151	0.220	0.315
	ΔlogR	0.000	0.852	1.431	0.494	-1.018	-1.459	-0.290	-1.709
	SE (ΔlogR)	0.167	0.216	0.182	0.210	0.302	0.192	0.249	0.336
	RE	1.000	7.112	26.977	3.119	0.096	0.035	0.513	0.020
G_{12}	logR	7.413	8.729	8.830	8.270	6.452	6.036	7.045	7.785
	SE (logR)	0.054	0.083	0.060	0.069	0.103	0.054	0.243	0.519

	ΔlogR	0.000	1.316	1.417	0.857	-0.961	-1.377	-0.368	0.372
	SE (ΔlogR)	0.076	0.099	0.081	0.088	0.116	0.076	0.249	0.521
	RE	1.000	20.701	26.122	7.194	0.109	0.042	0.429	2.355
G_{13}	logR	7.438	8.624	8.800	8.239	6.885	6.198	7.497	6.781
	SE (logR)	0.044	0.057	0.050	0.049	0.062	0.044	0.120	0.146
	ΔlogR	0.000	1.186	1.362	0.801	-0.553	-1.240	0.059	-0.657
	SE (ΔlogR)	0.062	0.072	0.067	0.066	0.076	0.062	0.127	0.152
	RE	1.000	15.346	23.014	6.324	0.280	0.058	1.146	0.220
G_{15}	logR	7.210	8.485	8.879	8.340	6.501	6.083	7.766	IA
	SE (logR)	0.089	0.189	0.103	0.119	0.185	0.083	0.521	IA
	ΔlogR	0.000	1.275	1.669	1.130	-0.709	-1.127	0.556	ND
	SE (ΔlogR)	0.125	0.208	0.136	0.149	0.205	0.121	0.529	ND
	RE	1.000	18.836	46.666	13.490	0.195	0.075	3.597	ND
β-arrestin1	logR	6.783	7.854	8.318	7.707	6.149	4.868	6.776	NC
	SE (logR)	0.088	0.134	0.165	0.135	0.212	0.069	0.348	NC
	ΔlogR	0.000	1.071	1.535	0.924	-0.634	-1.915	-0.007	ND
	SE (ΔlogR)	0.125	0.161	0.187	0.162	0.230	0.112	0.359	ND
	RE	1.000	11.776	34.277	8.395	0.232	0.012	0.984	ND
β-arrestin2	logR	7.017	8.086	8.344	7.834	6.208	5.321	7.086	5.547
	SE (logR)	0.025	0.034	0.038	0.032	0.049	0.022	0.121	0.299
	ΔlogR	0.000	1.069	1.327	0.817	-0.809	-1.696	0.069	-1.470
	SE (ΔlogR)	0.035	0.042	0.046	0.041	0.055	0.033	0.123	0.300
	RE	1.000	11.722	21.232	6.561	0.155	0.020	1.172	0.034

Table S15. CB1 bias factor (BF = $10^{\Delta\Delta logR}$) calculation as described in van der Weshuizen *et al.*, using WIN55212-2 as a reference ligand. ΔΔlogR=ΔlogR(pathway1) - ΔlogR(pathway2). ND = not determined.

pathways		WIN55,212-2	HU210	CP55940	nabilone	anandamide	2-AG	THC	cannabinol
G_{i2} - G_{i1}	ΔΔlogR	0.000	0.572	1.029	1.273	1.291	0.907	0.327	-0.267
	SE (ΔΔlogR)	0.151	0.175	0.181	0.185	0.278	0.188	0.192	0.292
	BF	1.000	3.733	**10.691**	**18.750**	**19.543**	8.072	2.123	0.541
G_{i2} - G_{i3}	ΔΔlogR	0.000	-0.339	-0.435	-0.705	-0.464	-0.270	-0.252	-0.475
	SE (ΔΔlogR)	0.172	0.169	0.168	0.175	0.188	0.189	0.235	0.416
	BF	1.000	0.458	0.367	0.197	0.344	0.537	0.560	0.335
G_{i2} - G_{oA}	ΔΔlogR	0.000	0.243	-0.290	-0.308	-0.179	0.305	-0.110	0.044
	SE (ΔΔlogR)	0.192	0.209	0.190	0.193	0.203	0.200	0.245	0.423
	BF	1.000	1.750	0.513	0.492	0.662	2.018	0.776	1.107
G_{i2} - G_{oB}	ΔΔlogR	0.000	0.039	0.097	-0.265	-0.114	0.275	0.001	0.252
	SE (ΔΔlogR)	0.164	0.174	0.163	0.168	0.179	0.171	0.223	0.305
	BF	1.000	1.094	1.250	0.543	0.769	1.884	1.002	1.786
G_{i2} - G_z	ΔΔlogR	0.000	0.468	0.058	0.343	0.277	0.464	0.715	0.993
	SE (ΔΔlogR)	0.206	0.248	0.218	0.244	0.328	0.230	0.300	0.411
	BF	1.000	2.938	1.143	2.203	1.892	2.911	5.188	**9.840**
G_{i2} - G_{12}	ΔΔlogR	0.000	0.004	0.072	-0.020	0.220	0.382	0.793	-1.088
	SE (ΔΔlogR)	0.143	0.156	0.145	0.152	0.172	0.148	0.299	0.573
	BF	1.000	1.009	1.180	0.955	1.660	2.410	6.209	**0.082**
G_{i2} - G_{13}	ΔΔlogR	0.000	0.134	0.127	0.036	-0.188	0.245	0.366	-0.059
	SE (ΔΔlogR)	0.136	0.141	0.137	0.141	0.148	0.141	0.209	0.281
	BF	1.000	1.361	1.340	1.086	0.649	1.758	2.323	0.873
G_{i2} - G_{15}	ΔΔlogR	0.000	0.045	-0.180	-0.293	-0.032	0.132	-0.131	ND
	SE (ΔΔlogR)	0.174	0.241	0.181	0.193	0.242	0.176	0.554	ND
	BF	1.000	1.109	0.661	0.509	0.929	1.355	0.740	ND
G_{i2} - β-arrestin1	ΔΔlogR	0.000	0.249	-0.046	-0.087	-0.107	0.920	0.432	ND
	SE (ΔΔlogR)	0.174	0.201	0.223	0.204	0.263	0.170	0.395	ND
	BF	1.000	1.774	0.899	0.818	0.782	8.318	2.704	ND
G_{i2} - β-arrestin2	ΔΔlogR	0.000	0.251	0.162	0.020	0.068	0.701	0.356	0.754
	SE (ΔΔlogR)	0.126	0.128	0.128	0.130	0.139	0.131	0.207	0.382
	BF	1.000	1.782	1.452	1.047	1.169	5.023	2.270	5.675
G_{oA} - G_{oB}	ΔΔlogR	0.000	-0.204	0.387	0.043	0.065	-0.030	0.111	0.208
	SE (ΔΔlogR)	0.186	0.212	0.184	0.187	0.202	0.192	0.233	0.400
	BF	1.000	0.625	2.438	1.104	1.161	0.933	1.291	1.614
G_{12} - G_{13}	ΔΔlogR	0.000	0.130	0.055	0.056	-0.408	-0.137	-0.427	1.029
	SE (ΔΔlogR)	0.099	0.123	0.105	0.110	0.138	0.098	0.279	0.543

	BF	1.000	1.349	1.135	1.138	0.391	0.729	0.374	**10.691**
β-arrestin1 – β-arrestin2	ΔΔlogR	0.000	0.002	0.208	0.107	0.175	-0.219	-0.076	ND
	SE (ΔΔlogR)	0.130	0.166	0.193	0.167	0.236	0.117	0.379	ND
	BF	1.000	1.005	1.614	1.279	1.496	0.604	0.839	ND

Table S16. Calculation of CB2 relative effectiveness (RE = $10^{\Delta logR}$) as described in van der Westhuizen *et al.*, using WIN55212-2 as a reference ligand. NC = not converged, ND = not determined. ΔlogR = logR(ligand) - logR(reference).

ligand		G_{i1}	G_{i2}	G_{i3}	G_{oA}	G_{oB}	β-arrestin1	β-arrestin2
WIN55,212-2	logR	9.409	9.414	9.318	9.061	9.202	9.062	9.259
	SE (logR)	0.075	0.063	0.062	0.059	0.060	0.152	0.081
	ΔlogR	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	SE (ΔlogR)	0.106	0.089	0.088	0.083	0.084	0.215	0.115
	RE	1.000	1.000	1.000	1.000	1.000	1.000	1.000
HU308	logR	8.131	8.008	7.912	7.784	7.914	7.242	7.400
	SE (logR)	0.095	0.088	0.058	0.061	0.092	0.199	0.089
	ΔlogR	-1.278	-1.406	-1.406	-1.277	-1.288	-1.820	-1.859
	SE (ΔlogR)	0.121	0.109	0.085	0.085	0.109	0.250	0.121
	RE	0.053	0.039	0.039	0.053	0.052	0.015	0.014
HU210	logR	9.314	9.467	9.210	9.076	9.457	9.103	9.043
	SE (logR)	0.081	0.063	0.062	0.070	0.063	0.160	0.107
	ΔlogR	-0.095	0.053	-0.108	0.015	0.255	0.041	-0.216
	SE (ΔlogR)	0.110	0.089	0.088	0.092	0.087	0.221	0.134
	RE	0.804	1.130	0.780	1.035	1.799	1.099	0.608
CP55940	logR	9.795	9.824	9.944	9.553	9.830	9.268	9.311
	SE (logR)	0.105	0.065	0.058	0.059	0.058	0.124	0.067
	ΔlogR	0.386	0.410	0.626	0.492	0.628	0.206	0.052
	SE (ΔlogR)	0.129	0.091	0.085	0.083	0.083	0.196	0.105
	RE	2.432	2.570	4.227	3.105	4.246	1.607	1.127
RO6843766	logR	9.089	8.768	8.877	8.756	9.028	9.277	8.892
	SE (logR)	0.114	0.092	0.095	0.148	0.081	0.444	0.234
	ΔlogR	-0.320	-0.646	-0.441	-0.305	-0.174	0.215	-0.367
	SE (ΔlogR)	0.137	0.112	0.113	0.159	0.101	0.470	0.248
	RE	0.479	0.226	0.362	0.495	0.670	1.641	0.430
RO6853457	logR	8.111	8.175	7.823	7.793	7.647	7.346	7.064
	SE (logR)	0.140	0.101	0.183	0.206	0.107	0.416	0.229
	ΔlogR	-1.298	-1.239	-1.495	-1.268	-1.555	-1.716	-2.195
	SE (ΔlogR)	0.158	0.119	0.194	0.214	0.123	0.443	0.243
	RE	0.050	0.058	0.032	0.054	0.028	0.019	0.006
RO7032019	logR	7.653	8.227	7.791	7.858	8.217	7.491	7.532
	SE (logR)	0.487	0.158	0.202	0.215	0.114	0.529	0.328
	ΔlogR	-1.756	-1.187	-1.527	-1.203	-0.985	-1.571	-1.727
	SE (ΔlogR)	0.492	0.170	0.211	0.223	0.129	0.550	0.338
	RE	0.018	0.065	0.030	0.063	0.104	0.027	0.019
RO6871487	logR	7.569	7.628	7.831	7.853	7.567	9.173	6.954
	SE (logR)	0.194	0.128	0.342	0.293	0.159	0.490	0.663
	ΔlogR	-1.840	-1.786	-1.487	-1.208	-1.635	0.111	-2.305

	SE (ΔlogR)	0.208	0.143	0.347	0.298	0.170	0.513	0.668
	RE	0.014	0.016	0.033	0.062	0.023	1.291	0.005
RO6878558	logR	7.700	7.654	7.473	7.613	7.579	7.834	6.853
	SE (logR)	0.124	0.100	0.154	0.172	0.082	0.553	0.349
	ΔlogR	-1.709	-1.760	-1.845	-1.448	-1.623	-1.228	-2.406
	SE (ΔlogR)	0.144	0.118	0.166	0.182	0.102	0.573	0.358
	RE	0.020	0.017	0.014	0.036	0.024	0.059	0.004
RO6883666	logR	7.632	7.242	7.186	8.010	7.399	NC	NC
	SE (logR)	0.170	0.124	0.363	0.441	0.136	ND	ND
	ΔlogR	-1.777	-2.172	-2.132	-1.051	-1.803	ND	ND
	SE (ΔlogR)	0.186	0.139	0.368	0.445	0.149	ND	ND
	RE	0.017	0.007	0.007	0.089	0.016	ND	ND
RO6853973	logR	8.595	8.754	8.409	8.294	8.564	10.010	8.202
	SE (logR)	0.186	0.201	0.486	0.401	0.218	0.621	1.082
	ΔlogR	-0.814	-0.660	-0.909	-0.767	-0.638	0.948	-1.057
	SE (ΔlogR)	0.200	0.211	0.490	0.405	0.226	0.640	1.085
	RE	0.153	0.219	0.123	0.171	0.230	8.872	0.088
RO6850007	logR	7.702	7.536	7.192	7.949	8.000	7.764	7.958
	SE (logR)	0.248	0.216	0.314	0.419	0.198	0.476	0.445
	ΔlogR	-1.707	-1.878	-2.126	-1.112	-1.202	-1.298	-1.301
	SE (ΔlogR)	0.259	0.225	0.320	0.423	0.206	0.500	0.453
	RE	0.020	0.013	0.007	0.077	0.063	0.050	0.050
RO6844395	logR	7.560	7.275	7.639	7.443	7.481	NC	7.056
	SE (logR)	0.141	0.087	0.160	0.129	0.078	ND	0.242
	ΔlogR	-1.849	-2.139	-1.679	-1.618	-1.721	ND	-2.203
	SE (ΔlogR)	0.159	0.108	0.171	0.142	0.098	ND	0.255
	RE	0.014	0.007	0.021	0.024	0.019	ND	0.006
RO6844112	logR	8.462	8.286	7.930	7.875	8.306	7.325	7.696
	SE (logR)	0.098	0.076	0.096	0.124	0.071	0.315	0.198
	ΔlogR	-0.947	-1.128	-1.388	-1.186	-0.896	-1.737	-1.563
	SE (ΔlogR)	0.123	0.098	0.115	0.138	0.093	0.350	0.214
	RE	0.113	0.074	0.041	0.065	0.127	0.018	0.027
RO5135445	logR	8.401	8.705	7.951	8.301	8.188	7.866	8.667
	SE (logR)	0.145	0.110	0.157	0.207	0.105	0.357	0.473
	ΔlogR	-1.008	-0.709	-1.367	-0.760	-1.014	-1.196	-0.592
	SE (ΔlogR)	0.163	0.127	0.169	0.215	0.120	0.388	0.480
	RE	0.098	0.195	0.043	0.174	0.097	0.064	0.256
RO6926274	logR	7.902	8.338	7.514	7.669	7.810	10.460	NC
	SE (logR)	0.309	0.206	0.294	0.430	0.345	0.398	ND
	ΔlogR	-1.507	-1.076	-1.804	-1.392	-1.392	1.398	ND
	SE (ΔlogR)	0.318	0.215	0.301	0.434	0.350	0.426	ND
	RE	0.031	0.084	0.016	0.041	0.041	25.003	ND
RO6892 033	logR	8.058	8.124	8.258	7.658	7.822	8.129	6.689
	SE (logR)	0.199	0.128	0.214	0.195	0.131	0.451	1.076
	ΔlogR	-1.351	-1.290	-1.060	-1.403	-1.380	-0.933	-2.570

	SE (ΔlogR)	0.212	0.142	0.223	0.204	0.144	0.476	1.079
	RE	0.045	0.051	0.087	0.040	0.042	0.117	0.003
RO6435559	logR	7.683	7.755	7.462	7.732	7.424	7.832	7.013
	SE (logR)	0.140	0.113	0.175	0.159	0.105	0.806	1.236
	ΔlogR	-1.726	-1.659	-1.856	-1.329	-1.778	-1.230	-2.246
	SE (ΔlogR)	0.158	0.129	0.186	0.170	0.121	0.820	1.239
	RE	0.019	0.022	0.014	0.047	0.017	0.059	0.006
RO6869094	logR	7.453	7.586	6.803	6.876	7.501	8.398	6.947
	SE (logR)	0.391	0.241	0.423	1.622	0.259	0.776	1.121
	ΔlogR	-1.956	-1.828	-2.515	-2.185	-1.701	-0.664	-2.312
	SE (ΔlogR)	0.398	0.249	0.428	1.623	0.266	0.791	1.124
	RE	0.011	0.015	0.003	0.007	0.020	0.217	0.005
FMP7234690	logR	7.731	8.046	7.406	7.081	7.811	7.926	7.518
	SE (logR)	0.127	0.111	0.092	0.130	0.084	0.388	0.185
	ΔlogR	-1.678	-1.368	-1.912	-1.980	-1.391	-1.136	-1.741
	SE (ΔlogR)	0.147	0.128	0.111	0.143	0.103	0.417	0.202
	RE	0.021	0.043	0.012	0.010	0.041	0.073	0.018
FMP7234691	logR	7.974	8.212	7.991	7.842	7.833	8.507	7.917
	SE (logR)	0.103	0.075	0.086	0.086	0.070	0.278	0.121
	ΔlogR	-1.435	-1.202	-1.327	-1.219	-1.369	-0.555	-1.342
	SE (ΔlogR)	0.127	0.098	0.106	0.104	0.092	0.316	0.146
	RE	0.037	0.063	0.047	0.060	0.043	0.279	0.045
FMP7234694	logR	7.639	8.024	7.832	8.097	8.033	7.486	7.815
	SE (logR)	0.115	0.074	0.082	0.082	0.074	0.425	0.132
	ΔlogR	-1.770	-1.390	-1.486	-0.964	-1.169	-1.576	-1.444
	SE (ΔlogR)	0.137	0.097	0.103	0.101	0.095	0.451	0.155
	RE	0.017	0.041	0.033	0.109	0.068	0.027	0.036
FMP7234698	logR	7.587	7.803	7.980	8.376	8.239	8.544	7.632
	SE (logR)	0.113	0.083	0.087	0.088	0.086	0.232	0.117
	ΔlogR	-1.822	-1.611	-1.338	-0.685	-0.963	-0.518	-1.627
	SE (ΔlogR)	0.136	0.104	0.107	0.106	0.104	0.278	0.143
	RE	0.015	0.024	0.046	0.207	0.109	0.303	0.024
FMP7234699	logR	7.672	7.777	7.658	8.256	7.704	7.818	7.717
	SE (logR)	0.129	0.075	0.099	0.093	0.071	0.230	0.148
	ΔlogR	-1.737	-1.637	-1.660	-0.805	-1.498	-1.244	-1.542
	SE (ΔlogR)	0.149	0.098	0.117	0.110	0.093	0.276	0.169
	RE	0.018	0.023	0.022	0.157	0.032	0.057	0.029
JWH133	logR	8.653	7.697	8.274	8.032	8.481	8.107	7.835
	SE (logR)	0.107	0.063	0.057	0.059	0.056	0.131	0.072
	ΔlogR	-0.756	-1.717	-1.044	-1.029	-0.721	-0.955	-1.424
	SE (ΔlogR)	0.130	0.089	0.084	0.083	0.082	0.201	0.109
	RE	0.175	0.019	0.090	0.094	0.190	0.111	0.038
(*rac*)-AM1241	logR	8.038	7.615	7.483	7.457	7.822	7.401	7.154
	SE (logR)	0.134	0.103	0.158	0.221	0.091	0.396	0.427
	ΔlogR	-1.371	-1.799	-1.835	-1.604	-1.380	-1.661	-2.105

	SE (ΔlogR)	0.153	0.120	0.169	0.229	0.109	0.424	0.435
	RE	0.043	0.016	0.015	0.025	0.042	0.022	0.008
(R)-AM1241	logR	8.020	7.835	7.899	7.974	7.744	8.477	7.647
	SE (logR)	0.122	0.105	0.145	0.254	0.096	0.530	0.286
	ΔlogR	-1.389	-1.579	-1.419	-1.087	-1.458	-0.585	-1.612
	SE (ΔlogR)	0.143	0.122	0.158	0.260	0.113	0.552	0.298
	RE	0.041	0.026	0.038	0.082	0.035	0.260	0.024
(S)-AM1241	logR	7.264	7.120	7.215	6.812	7.138	6.862	6.425
	SE (logR)	0.100	0.073	0.075	0.096	0.071	0.280	0.123
	ΔlogR	-2.145	-2.294	-2.103	-2.249	-2.064	-2.200	-2.834
	SE (ΔlogR)	0.125	0.097	0.097	0.113	0.093	0.318	0.147
	RE	0.007	0.005	0.008	0.006	0.009	0.006	0.001
nabilone	logR	8.782	8.920	8.907	8.283	8.629	8.445	8.444
	SE (logR)	0.081	0.077	0.062	0.059	0.060	0.176	0.102
	ΔlogR	-0.627	-0.494	-0.411	-0.778	-0.573	-0.617	-0.815
	SE (ΔlogR)	0.110	0.100	0.088	0.083	0.085	0.232	0.130
	RE	0.236	0.321	0.388	0.167	0.267	0.242	0.153
THC	logR	7.556	7.296	7.229	7.838	7.541	NC	7.409
	SE (logR)	0.237	0.162	0.196	0.345	0.145	ND	0.564
	ΔlogR	-1.853	-2.118	-2.089	-1.223	-1.661	ND	-1.850
	SE (ΔlogR)	0.248	0.173	0.206	0.350	0.156	ND	0.570
	RE	0.014	0.008	0.008	0.060	0.022	ND	0.014
cannabinol	logR	7.430	7.039	6.960	7.895	7.202	5.678	5.681
	SE (logR)	0.160	0.126	0.138	0.191	0.116	0.975	0.562
	ΔlogR	-1.979	-2.375	-2.358	-1.166	-2.000	-3.384	-3.578
	SE (ΔlogR)	0.177	0.141	0.151	0.200	0.130	0.987	0.568
	RE	0.010	0.004	0.004	0.068	0.010	0.000	0.000
anandamide	logR	7.233	6.935	6.930	6.808	7.343	5.164	5.980
	SE (logR)	0.098	0.077	0.092	0.118	0.080	0.103	0.179
	ΔlogR	-2.176	-2.479	-2.388	-2.253	-1.859	-3.898	-3.279
	SE (ΔlogR)	0.123	0.100	0.111	0.132	0.100	0.183	0.196
	RE	0.007	0.003	0.004	0.006	0.014	0.000	0.001
2-AG	logR	6.941	6.692	6.700	6.706	7.002	6.046	5.979
	SE (logR)	0.080	0.066	0.060	0.075	0.064	0.108	0.062
	ΔlogR	-2.468	-2.722	-2.618	-2.355	-2.200	-3.016	-3.280
	SE (ΔlogR)	0.110	0.091	0.086	0.096	0.087	0.186	0.102
	RE	0.003	0.002	0.002	0.004	0.006	0.001	0.001

Table S17. CB2 bias factor (BF = $10^{\Delta\Delta\log R}$) calculation as described in van der Weshuizen *et al*., using WIN55212-2 as a reference ligand. ΔΔlogR = ΔlogR(pathway1) - ΔlogR(pathway2). ND = not determined.

ligand		G_{i2} – G_{i1}	G_{i2} – G_{i3}	G_{i2} – G_{oA}	G_{i2} – G_{oB}	G_{i2} – β-arrestin1	G_{i2} – β-arrestin2	G_{oB} – G_{oA}	G_{oB} – β-arrestin2	β-arrestin1 – β-arrestin2
WIN55,212-2	ΔΔlogR	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	SE (ΔΔlogR)	0.138	0.125	0.122	0.123	0.232	0.146	0.119	0.143	0.244
	BF	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
HU308	ΔΔlogR	-0.128	0.000	-0.129	-0.118	0.414	0.453	-0.011	0.571	0.039
	SE (ΔΔlogR)	0.163	0.138	0.138	0.154	0.273	0.163	0.139	0.163	0.278
	BF	0.745	1.000	0.743	0.762	2.594	2.838	0.975	3.724	1.094
HU210	ΔΔlogR	0.148	0.161	0.038	-0.202	0.012	0.269	0.240	0.471	0.257
	SE (ΔΔlogR)	0.142	0.125	0.128	0.124	0.238	0.161	0.126	0.160	0.258
	BF	1.406	1.449	1.091	0.628	1.028	1.858	1.738	2.958	1.807
CP55940	ΔΔlogR	0.024	-0.216	-0.082	-0.218	0.204	0.358	0.136	0.576	0.154
	SE (ΔΔlogR)	0.157	0.124	0.123	0.123	0.216	0.139	0.118	0.134	0.223
	BF	1.057	0.608	0.828	0.605	1.600	2.280	1.368	3.767	1.426
RO6843766	ΔΔlogR	-0.326	-0.205	-0.341	-0.472	-0.861	-0.279	0.131	0.193	0.582
	SE (ΔΔlogR)	0.177	0.159	0.194	0.150	0.483	0.272	0.188	0.268	0.531
	BF	0.472	0.624	0.456	0.337	0.138	0.526	1.352	1.560	3.819
RO6853457	ΔΔlogR	0.059	0.256	0.029	0.316	0.477	0.956	-0.287	0.640	0.479
	SE (ΔΔlogR)	0.198	0.227	0.245	0.171	0.459	0.271	0.247	0.273	0.506
	BF	1.146	1.803	1.069	2.070	2.999	**9.036**	0.516	4.365	3.013
RO7032019	ΔΔlogR	0.569	0.340	0.016	-0.202	0.384	0.540	0.218	0.742	0.156
	SE (ΔΔlogR)	0.521	0.271	0.281	0.213	0.576	0.378	0.258	0.361	0.645
	BF	3.707	2.188	1.038	0.628	2.421	3.467	1.652	5.521	1.432
RO6871487	ΔΔlogR	0.054	-0.299	-0.578	-0.151	-1.897	0.519	-0.427	0.670	2.416
	SE (ΔΔlogR)	0.253	0.375	0.331	0.222	0.533	0.683	0.344	0.689	0.842
	BF	1.132	0.502	0.264	0.706	**0.013**	3.304	0.374	4.677	**260.615**
RO6878558	ΔΔlogR	-0.051	0.085	-0.312	-0.137	-0.532	0.646	-0.175	0.783	1.178
	SE (ΔΔlogR)	0.187	0.203	0.217	0.156	0.585	0.377	0.208	0.372	0.676
	BF	0.889	1.216	0.488	0.729	0.294	4.426	0.668	6.067	15.066
R C	ΔΔlogR	-0.395	-0.040	-1.121	-0.369	ND	ND	-0.752	ND	ND

	SE (ΔΔlogR)	0.232	0.393	0.466	0.203	ND	ND	0.469	ND	ND
	BF	0.403	0.912	**0.076**	0.428	ND	ND	0.177	ND	ND
RO6853973	ΔΔlogR	0.154	0.249	0.107	-0.022	-1.608	0.397	0.129	0.419	2.005
	SE (ΔΔlogR)	0.291	0.534	0.456	0.309	0.673	1.105	0.464	1.108	1.260
	BF	1.426	1.774	1.279	0.951	**0.025**	2.495	1.346	2.624	101.158
RO6850007	ΔΔlogR	-0.171	0.248	-0.766	-0.676	-0.580	-0.577	-0.090	0.099	0.003
	SE (ΔΔlogR)	0.343	0.391	0.479	0.305	0.548	0.505	0.471	0.497	0.674
	BF	0.675	1.770	0.171	0.211	0.263	0.265	0.813	1.256	1.007
RO6844395	ΔΔlogR	-0.290	-0.460	-0.521	-0.418	ND	0.064	-0.103	0.482	ND
	SE (ΔΔlogR)	0.192	0.202	0.178	0.146	ND	0.277	0.172	0.273	ND
	BF	0.513	0.347	0.301	0.382	ND	1.159	0.789	3.034	ND
RO6844112	ΔΔlogR	-0.181	0.260	0.058	-0.232	0.609	0.435	0.290	0.667	-0.174
	SE (ΔΔlogR)	0.158	0.151	0.169	0.135	0.363	0.236	0.166	0.233	0.410
	BF	0.659	1.820	1.143	0.586	4.064	2.723	1.950	4.645	0.670
RO5135445	ΔΔlogR	0.299	0.658	0.051	0.305	0.487	-0.117	-0.254	-0.422	-0.604
	SE (ΔΔlogR)	0.207	0.211	0.250	0.175	0.408	0.496	0.247	0.495	0.617
	BF	1.991	4.550	1.125	2.018	3.069	0.764	0.557	0.378	0.249
RO6926274	ΔΔlogR	0.431	0.728	0.316	0.316	-2.474	ND	0.000	ND	ND
	SE (ΔΔlogR)	0.384	0.370	0.484	0.411	0.477	ND	0.558	ND	ND
	BF	2.698	5.346	2.070	2.070	**0.003**	ND	1.000	ND	ND
RO6892033	ΔΔlogR	0.061	-0.230	0.113	0.090	-0.357	1.280	0.023	1.190	1.637
	SE (ΔΔlogR)	0.255	0.264	0.248	0.202	0.496	1.088	0.249	1.089	1.179
	BF	1.151	0.589	1.297	1.230	0.440	19.055	1.054	15.488	43.351
RO6435559	ΔΔlogR	0.067	0.197	-0.330	0.119	-0.429	0.587	-0.449	0.468	1.016
	SE (ΔΔlogR)	0.204	0.226	0.213	0.177	0.830	1.245	0.209	1.245	1.485
	BF	1.167	1.574	0.468	1.315	0.372	3.864	0.356	2.938	10.375
RO6869094	ΔΔlogR	0.128	0.687	0.357	-0.127	-1.164	0.484	0.484	0.611	1.648
	SE (ΔΔlogR)	0.470	0.495	1.642	0.365	0.829	1.151	1.645	1.155	1.374
	BF	1.343	4.864	2.275	0.746	0.069	3.048	3.048	4.083	44.463
FMP7234690	ΔΔlogR	0.310	0.544	0.612	0.023	-0.232	0.373	0.589	0.350	0.605
	SE (ΔΔlogR)	0.195	0.169	0.191	0.164	0.436	0.239	0.176	0.227	0.463
	BF	2.042	3.499	4.093	1.054	0.586	2.360	3.882	2.239	4.027
FMP7234691	ΔΔlogR	0.233	0.125	0.017	0.167	-0.647	0.140	-0.150	-0.027	0.787
	SE (ΔΔlogR)	0.161	0.145	0.143	0.135	0.331	0.176	0.139	0.172	0.348

	BF	1.710	1.334	1.040	1.469	0.225	1.380	0.708	0.940	6.124
FMP7234694	ΔΔlogR	0.380	0.096	-0.426	-0.221	0.186	0.054	-0.205	0.275	-0.132
	SE (ΔΔlogR)	0.168	0.142	0.140	0.136	0.462	0.183	0.139	0.182	0.477
	BF	2.399	1.247	0.375	0.601	1.535	1.132	0.624	1.884	0.738
FMP7234698	ΔΔlogR	0.211	-0.273	-0.926	-0.648	-1.093	0.016	-0.278	0.664	1.109
	SE (ΔΔlogR)	0.171	0.149	0.148	0.147	0.296	0.177	0.148	0.177	0.312
	BF	1.626	0.533	0.119	0.225	**0.081**	1.038	0.527	4.613	**12.853**
FMP7234699	ΔΔlogR	0.100	0.023	-0.832	-0.139	-0.393	-0.095	-0.693	0.044	0.298
	SE (ΔΔlogR)	0.178	0.153	0.147	0.135	0.293	0.195	0.144	0.193	0.323
	BF	1.259	1.054	0.147	0.726	0.405	0.804	0.203	1.107	1.986
JWH133	ΔΔlogR	-0.961	-0.673	-0.688	-0.996	-0.762	-0.293	0.308	0.703	0.469
	SE (ΔΔlogR)	0.158	0.123	0.122	0.121	0.220	0.141	0.117	0.136	0.228
	BF	**0.109**	0.212	0.205	**0.101**	**0.173**	0.509	2.032	5.047	2.944
(*rac*)-AM1241	ΔΔlogR	-0.428	0.036	-0.195	-0.419	-0.138	0.306	0.224	0.725	0.444
	SE (ΔΔlogR)	0.195	0.208	0.258	0.162	0.441	0.451	0.253	0.448	0.607
	BF	0.373	1.086	0.638	0.381	0.728	2.023	1.675	5.309	2.780
(*R*)-AM1241	ΔΔlogR	-0.190	-0.160	-0.492	-0.121	-0.994	0.033	-0.371	0.154	1.027
	SE (ΔΔlogR)	0.188	0.199	0.288	0.167	0.565	0.322	0.284	0.318	0.627
	BF	0.646	0.692	0.322	0.757	0.101	1.079	0.426	1.426	10.641
(*S*)-AM1241	ΔΔlogR	-0.149	-0.191	-0.045	-0.230	-0.094	0.540	0.185	0.770	0.634
	SE (ΔΔlogR)	0.158	0.137	0.149	0.134	0.333	0.176	0.146	0.174	0.351
	BF	0.710	0.644	0.902	0.589	0.805	3.467	1.531	5.888	4.305
nabilone	ΔΔlogR	0.133	-0.083	0.284	0.079	0.123	0.321	0.205	0.242	0.198
	SE (ΔΔlogR)	0.148	0.133	0.130	0.131	0.253	0.164	0.119	0.155	0.266
	BF	1.358	0.826	1.923	1.199	1.327	2.094	1.603	1.746	1.578
THC	ΔΔlogR	-0.265	-0.029	-0.895	-0.457	ND	-0.268	-0.438	0.189	ND
	SE (ΔΔlogR)	0.303	0.269	0.391	0.234	ND	0.596	0.384	0.591	ND
	BF	0.543	0.935	0.127	0.349	ND	0.540	0.365	1.545	ND
cannabinol	ΔΔlogR	-0.396	-0.017	-1.209	-0.375	1.009	1.203	-0.834	1.578	0.194
	SE (ΔΔlogR)	0.226	0.207	0.245	0.192	0.997	0.585	0.239	0.582	1.138
	BF	0.402	0.962	**0.062**	0.422	10.209	15.959	**0.147**	**37.844**	1.563
anandamide	ΔΔlogR	-0.303	-0.091	-0.226	-0.620	1.419	0.800	0.394	1.420	-0.619
	SE (ΔΔlogR)	0.158	0.149	0.165	0.141	0.209	0.220	0.165	0.220	0.269

	BF	0.498	0.811	0.594	0.240	**26.242**	6.310	2.477	**26.303**	0.240
2-AG	ΔΔlogR	-0.254	-0.104	-0.367	-0.522	0.294	0.558	0.155	1.080	0.264
	SE (ΔΔlogR)	0.142	0.126	0.132	0.126	0.207	0.137	0.129	0.134	0.212
	BF	0.557	0.787	0.430	0.301	1.968	3.614	1.429	**12.023**	1.837