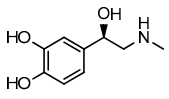
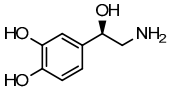
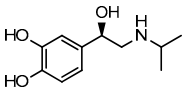
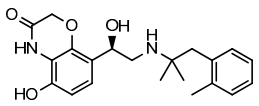
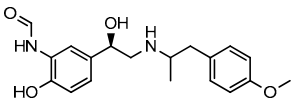
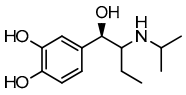
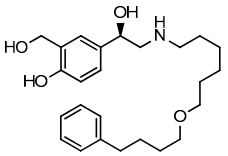
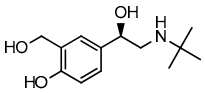
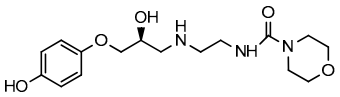
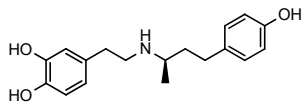
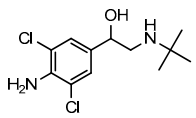
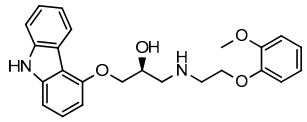
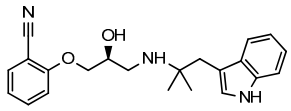
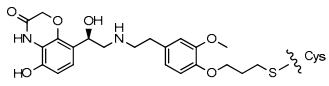
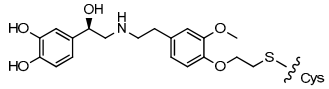
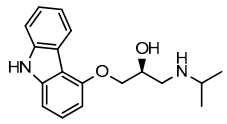
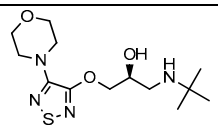
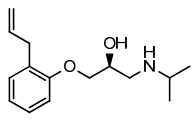
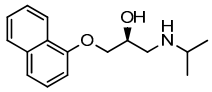
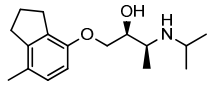
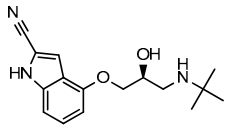
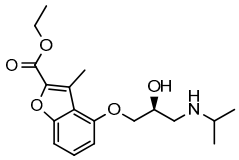
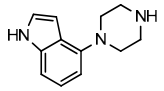
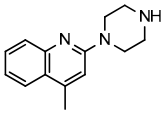
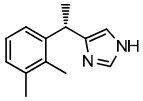
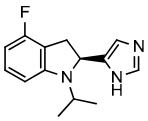
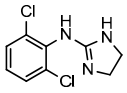
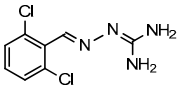
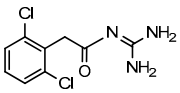
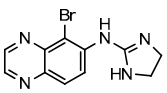
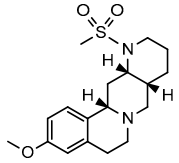
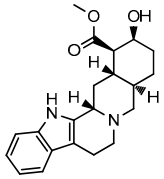
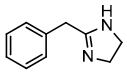
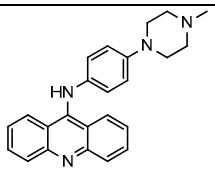
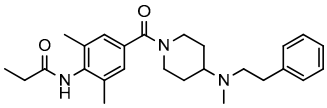
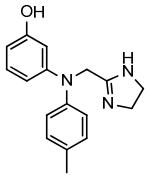
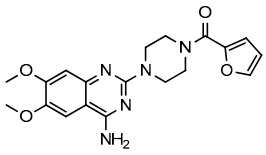
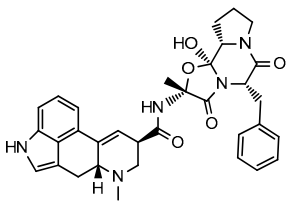
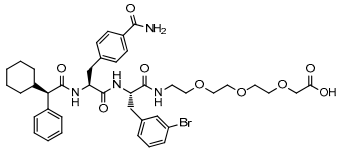
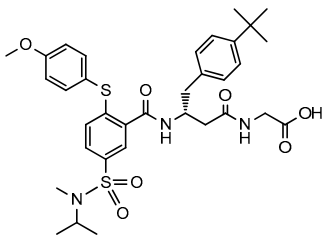
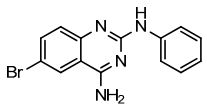
Table S1. Representative ligands used in structural studies of adrenergic receptors.

Compound name	Structural formula	Status	Representative PDB	Function	Selectivity[a]
Epinephrine ((−)-adrenaline)		Approved drug	β_2: 4LDO (Nb)[1] β_1: 7BTS (human, Nb)[2]	Agonist	α_1, α_2, β (see Figure 1 for detail)
Norepinephrine ((−)-noradrenaline)		Approved drug	β_1: 7BU6 (human, Nb)[2]	Agonist	α_1, α_2, β (see Figure 1 for detail)
Isoproterenol (isoprenaline)		Approved drug	β_2: 7DHR (G_s)[3] β_1: 7JJO (G_s)[4], 7BU7 (human, Nb)[2], 6H7J (Nb)[5], 2Y03[6]	Agonist	β [7-9]
BI-167107		Research	β_2: 3SN6[10] (G_s), 3P0G (Nb)[11] β_1: 7BU7 (human, Nb)[2]	Agonist (arrestin-biased[12])	β (no data for subtype selectivity)
Formoterol		Approved drug	β_2: 7BZ2 (G_s)[13] β_1: 6TKO (arrestin), 6IBL (Nb)[14]	Agonist (arrestin-biased[15])	$\beta_2 > \beta_1$, β_3 [9,16,17]
Isoetharine		Approved drug	/	Agonist (arrestin-biased in β_2AR[18], G_s-biased in β_1AR[19])	β_1, β_2 [19,20] (no data for β_3AR)
Salmeterol		Approved drug	β_2: 6MXT(Nb)[21]	Partial agonist (G_s-biased)	β_2 [9,22]
Salbutamol		Approved drug	β_2: 7DHI (G_s)[3] β_1: 6H7M (Nb), 2Y04[6]	Partial agonist	$\beta_2 > \beta_1$, β_3 [9,22]
Xamoterol (ICI-118587)		Approved drug	β_1: 6H7N (Nb)[5]	Partial agonist	$\beta_1 > \beta_2 > \beta_3$ [9,22]

Compound name	Structural formula	Status	Representative PDB	Function	Selectivity[a]
Dobutamine		Approved drug	β_1: 2Y00[6], 2Y01[6]	Partial agonist	β [9,16,23]; enantiomer is selective for α_1 [24,25]
Clenbuterol		Research	/	Partial agonist	$\beta_2 > \beta_1 > \beta_3$ [9]
Carvedilol		Approved drug	β_2: 6PS3[26] β_1: 4AMJ[27]	G_s antagonist & arrestin agonist[28]	β [22]
Bucindolol		Clinical trial phase 2	β_1: 4AMI[27]	G_s antagonist & arrestin agonist[29]; antagonist of α_1ARs	β_1, $\beta_2 > \beta_3$ [9]; α_1 [30,31]
FAUC50		Research	β_2: 3PDS[32]	Covalent agonist	β (no data for subtype selectivity)
'2' [33]		Research	β_2: 4QKX[33]	Covalent agonist	β (no data for subtype selectivity)
Carazolol		Approved drug	β_2: 2RH1[34] β_1: 7BVQ (human, Nb)[2], 2YCW[35]	Inverse agonist of β_1 & β_2; agonist of β_3 [36]	β_1, $\beta_2 > \beta_3$ [9]
Timolol		Approved drug	β_2: 3D4S[37], 6PS1[26], 6PS6[26]	Inverse agonist	$\beta_2 > \beta_1 > \beta_3$ [22]
Alprenolol		Approved drug	β_2: 3NYA[38], 6PS2[26], 6PRZ[26]	Antagonist	$\beta_2 > \beta_1$, β_3 [22]
Propranolol		Approved drug	β_2: 6PS5[26]	Antagonist	β_1, $\beta_2 > \beta_3$ [22]
ICI 118551		Research	β_2: 3NY8[38], 6PS4[26]	Inverse agonist	$\beta_2 >> \beta_1$, β_3 [22]

Compound name	Structural formula	Status	Representative PDB	Function	Selectivity[a]
Cyanopindolol		Research	β_1: 6H7O (Nb)[5], 2VT4[39]	Antagonist & weak partial agonist [6H7O]	β_1, β_2 >> β_3 [9]
'2' [38] / '1' [40]		Research (discovered through docking virtural screening[40])	β_2: 3NY9[38]	Inverse agonist	β_2 (no data for other subtypes)
'19' [41]		Research (discovered through SPR screening from fragment library[41])	β_1: 3ZPQ[41]	Antagonist	β_1 (no data for other subtypes)
'20' [41]		Research (discovered through SPR screening from fragment library[41])	β_1: 3ZPR[41]	Antagonist	β_1 (no data for other subtypes)
Dexmedetomidine		Approved drug	α_{2B}: 6K41 (Gi) , 6K42 (Go)[42]	Partial agonist of α_{2A}; full agonist of α_{2B} & α_{2C}	α_2 [43] [44]
RES		Research	α_{2A}: 6KUY[45]	Partial agonist	α_2 (no data for subtype selectivity)
Clonidine		Approved drug	/	Partial agonist	α_2 >> α_1 [43,44]
Guanabenz		Approved drug	/	Partial agonist of α_{2A} & α_{2B}; antagonist of α_{2C}	α_{2A} > α_{2B}, α_{2C} [44,46]
Guanfacine		Approved drug	/	Partial agonist	α_2 >> α_1, α_{2A} > α_{2B}, α_{2C} [44,46]
Brimonidine (UK 14,304)		Approved drug	/	Full agonist of α_{2A}; partial agonist of α_{2B} & α_{2C}	α_2 >> α_1 [43,44]

Compound name	Structural formula	Status	Representative PDB	Function	Selectivity[a]
RS 79948		Research	α_{2A}: 6KUX[45] α_{2C}: 6KUW[47]	Antagonist	α_2 [48]
Yohimbine		Approved drug	/	Antagonist	α_2 [49]
Tolazoline		Approved drug	/	Antagonist	$\alpha_{2A} > \alpha_{2B}$, α_{2C} [44]
JP1302		Research	/	Antagonist	$\alpha_{2C} > \alpha_{2A}$, α_{2B} [50]
OPC-28326		Research	/	Antagonist	$\alpha_{2C} > \alpha_{2A}$, α_{2B} [51]
Phentolamine		Approved drug	/	Antagonist	α_1, α_2 [49,52]
Prazosin		Approved drug	/	Antagonist	$\alpha_1 >> \alpha_2$ [44,53,54]
Ergotamine		Approved drug	/	Antagonist	$\alpha_2 > \alpha_1 > \beta$ [55]
Cmpd-15PA		Research	β_2: 5X7D[56]	NAM	β_2 [56]
Cmpd-6FA		Research	β_2: 6N48 (Nb)[57]	PAM	$\beta_2 > \beta_1$ [57]

Compound name	Structural formula	Status	Representative PDB	Function	Selectivity[a]
AS408		Research	β_2: 6OBA[58]	NAM	$\beta_2 > \beta_1$ [58]

[a]Selective, more than 1000 folds or no effect in unpreferred types/subtypes; >>, 100 to 1000 folds; >, 10 to 100 folds; non-selective, less than 10 folds.

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