Electronic Supplementary Material (ESI) for RSC Medicinal Chemistry.

Supplementary data

Tables with bias factors

MOR ligand	Biased pathway	Bias factor (β)	10^{β} (equation 2)	Reference ligand	Calculation of bias	Assay[a]	Reference
TRV-130	G protein	3.00	/	Morphine	RA_i	cAMP vs β-arrestin-2	DeWire, J. Pharmacol. Exp. Ther., 2013
	G protein	1.64	43.65	Morphine	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Burgueno, Sci. Rep., 2017
Morphine	β-arrestin	-0.99	0.10	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2	Thompson, Mol. Pharmacol., 2015
	β-arrestin	-0.13	0.75	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Thompson, Mol. Pharmacol., 2015
	G protein	0.11	1.3	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	β-arrestin	-0.21	0.62	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	β-arrestin	-0.09	0.80	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (CHO cells)	Schmid, Cell, 2017
	G protein	0.29	1.9	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (brain cells)	Schmid, Cell, 2017
Buprenorphine	G protein	1.84	69.2	Morphine	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Burgueno, Sci. Rep., 2017
Kurkinorin	G protein	0.57	/	**DAMGO**	$\Delta\Delta\log(RA)$	β-arrestin-2 vs cAMP	Crowley, J. Med. Chem., 2016
Herkamide	G protein	0.32	/	**DAMGO**	$\Delta\Delta\log(RA)$	β-arrestin-2 vs cAMP	Crowley, J. Med. Chem., 2016
SR-11501	β-arrestin	-0.39	0.41	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	β-arrestin	-0.09	0.81	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	β-arrestin	-0.91	0.12	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (CHO cells)	Schmid, Cell, 2017
	β-arrestin	-0.64	0.23	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (brain cells)	Schmid, Cell, 2017
SR-14968	G protein	1.55	36	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	0.71	5.1	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	0.83	6.7	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (CHO cells)	Schmid, Cell, 2017

[a] All assays are performed on human receptor, expect if stated otherwise

	G protein	1.54	34	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (brain cells)	Schmid, Cell, 2017
SR-14969	G protein	1.03	11	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	0.40	2.5	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	0.46	2.9	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (CHO cells)	Schmid, Cell, 2017
	G protein	0.93	8.6	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (brain cells)	Schmid, Cell, 2017
SR-15098	G protein	1.47	29	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	1.28	19	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	1.03	11	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (CHO cells)	Schmid, Cell, 2017
	G protein	1.74	55	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (brain cells)	Schmid, Cell, 2017
SR-15099	G protein	1.68	47	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	1.44	27	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	1.07	12	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (CHO cells)	Schmid, Cell, 2017
	G protein	1.74	55	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (brain cells)	Schmid, Cell, 2017
SR-17018	G protein	1.93	85	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	1.60	40	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	1.47	30	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (CHO cells)	Schmid, Cell, 2017
	G protein	2.01	102	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (brain cells)	Schmid, Cell, 2017
41	G protein	1.36	23	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2	Kennedy, J. Med. Chem., 2018
44	G protein	1.75	56	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2	Kennedy, J. Med. Chem., 2018
Endomorphin-1	β-arrestin	-1.224	0.06	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2	Thompson, Mol. Pharmacol., 2015
	G protein	0.614	4.11	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Thompson, Mol. Pharmacol., 2015
	β-arrestin	-0.286	0.52	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-1	Thompson, Mol. Pharmacol., 2015
	G protein	1.552	35.6	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-1	Thompson, Mol. Pharmacol., 2015
Endomorphin-2	β-arrestin	-0.56	0.27	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2	Thompson, Mol. Pharmacol., 2015
	G protein	0.59	3.93	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Thompson, Mol. Pharmacol., 2015
	β-arrestin	-0.82	0.15	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-1	Thompson, Mol. Pharmacol., 2015

	G protein	0.33	2.15	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-1	Thompson, Mol. Pharmacol., 2015
Fentanyl	β-arrestin	-0.7	0.18	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	0.45	2.8	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	β-arrestin	-1.27	0.05	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (CHO cells)	Schmid, Cell, 2017
	β-arrestin	-0.83	0.15	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (brain cells)	Schmid, Cell, 2017
	G protein	0.96	9.1	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Burgueno, Sci. Rep., 2017
Sufentanil	β-arrestin	-0.78	0.16	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	G protein	0.02	1.1	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2 (CHO cells)	Schmid, Cell, 2017
	β-arrestin	-1.25	0.06	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (CHO cells)	Schmid, Cell, 2017
	β-arrestin	-0.85	0.14	**DAMGO**	$\Delta\Delta\log(\tau/K_A)$	GTPγS (mMOR) vs β-arrestin-2 (mMOR) (brain cells)	Schmid, Cell, 2017

DOR ligand	**Biased pathway**	**Bias factor (β)**	**10^{β} (equation 2)**	**Reference ligand**	**Calculation of bias**	**Assay**	**Reference**
Rubiscolin-5	G protein	0.31	2.04	Leu-ENK	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Cassell, Eur. Neuropharmacol., 2019
Rubiscolin-6	β-arrestin	-0.28	0.52	Leu-ENK	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Cassell, Eur. Neuropharmacol., 2019
DADLE	G protein	1.5	31.6	**SNC-80**	$\Delta\Delta\log(\tau/K_A)$	$G_{\alpha i}$ BRET vs β-arrestin-1	Conibear, J. Pharmacol. Exp. Ther., 2020
	G protein	1.15	14.1	**SNC-80**	$\Delta\Delta\log(\tau/K_A)$	$G_{\alpha i}$ BRET vs β-arrestin-2	Conibear, J. Pharmacol. Exp. Ther., 2020
UFP-512	G protein	2.12	132	**DPDPE**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs internalization	Charfi, Cell. Mol. Life Sci., 2014
SNC-80	G protein	1.70	50	**DPDPE**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs internalization	Charfi, Cell. Mol. Life Sci., 2014
PN6047	G protein	1.17	14.8	**SNC-80**	$\Delta\Delta\log(\tau/K_A)$	$G_{\alpha i}$ BRET vs β-arrestin-1	Conibear, J. Pharmacol. Exp. Ther.,2020
	G protein	0.885	7.5	**SNC-80**	$\Delta\Delta\log(\tau/K_A)$	$G_{\alpha i}$ BRET vs β-arrestin-2	Conibear, J. Pharmacol. Exp. Ther.,2020
ARM390	G protein	0.55	3.9	**SNC-80**	$\Delta\Delta\log(\tau/K_A)$	$G_{\alpha i}$ BRET vs β-arrestin-2	Conibear, J. Pharmacol. Exp. Ther.,2020
TAN-67	G protein	-1.4	/	Leu-ENK	$\Delta\Delta\log(RA)$	β-arrestin-2 vs cAMP	Robins, Front. Psychiatry, 2018
BMS-986187	G protein	1.53	34	**SNC-80**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2	Stanczyk, Br. J. Pharmacol., 2019

KOR ligand	Biased pathway	Bias factor (β)	10^{β} (equation 2)	Reference ligand	Calculation of bias	Assay	Reference
Triazole 1.1	G protein	1.79	61.2	**U69.593**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (enzyme fragment complementation)	Zhou, J. Biol. Chem., 2013
	G protein	1.3	20	**U69.593**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (imaging)	Zhou, J. Biol. Chem., 2013
Triazole 1.5	G protein	2.05	111.7	**U69.593**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (EFC)	Zhou, J. Biol. Chem., 2013
	G protein	2.00	100	**U69.593**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (imaging)	Zhou, J. Biol. Chem., 2013
1.2	G protein	1.9	122	**U69.593**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2	Lovell, ACS Chem. Neurosci., 2015
6'-GNTI	G protein	0.76	6	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	White, Mol. Pharmacol., 2014
RB-64	G protein	1.55	35	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	White, Mol. Pharmacol., 2014
	G protein	1.98	96	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	cAMP (mKOR) vs β-arrestin (mKOR)	White, J. Pharmacol., 2015
Nalfurafine	G protein	1.15	/	**U50,488**	ΔΔlog(RA)	ERK1/2 phosphorylation (rKOR) vs p38 phosphorylation (rKOR)	Schattauer, Cell. Signal., 2017
	G protein	3.2	/	**U50,488**	ΔΔlog(RA)	ERK1/2 phosphorylation vs p38 phosphorylation	Schattauer, Cell. Signal., 2017
Mesyl Sal B	G protein	0.61	/	**U50,488**	ΔΔlog(RA)	cAMP vs β-arrestin-2	Kivell, Molecules, 2018
GR89696	β-arrestin	0.67	5	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	β-arrestin-2 vs cAMP	White, Mol. Pharmacol., 2014
U50.488	G protein	0.91	8	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	White, Mol. Pharmacol., 2014
	G protein	0.6	/	**U69.593**	Δlog(RA)	GTPγS vs β-arrestin-2	Dunn, Int. J. Neuropharmacol., 2018
(-) U50.488	β-arrestin	0.31	2	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	β-arrestin-2 vs cAMP	White, Mol. Pharmacol., 2014
BPHA	G protein	1.8	/	**U69.593**	Δlog(RA)	GTPγS vs β-arrestin-2	Dunn, Int. J. Neuropharmacol., 2018
MCBPHA	G protein	1.6	/	**U69.593**	Δlog(RA)	GTPγS vs β-arrestin-2	Dunn, Int. J. Neuropharmacol., 2018
MCPPHA	G protein	1.3	/	**U69.593**	Δlog(RA)	GTPγS vs β-arrestin-2	Dunn, Int. J. Neuropharmacol., 2018
Dyn A	G protein	1.56	34	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	White, Mol. Pharmacol., 2014
Dyn 1-8	G protein	0.68	4	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	White, Mol. Pharmacol., 2014
Dyn 1-9	G protein	1.22	16	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	White, Mol. Pharmacol., 2014
Dyn 1-11	G protein	1.67	44	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	White, Mol. Pharmacol., 2014
Dyn 1-13	G protein	1.56	34	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	White, Mol. Pharmacol., 2014
Isoquinoline 2.1	G protein	1.50	31.4	**U69.593**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (EFC)	Zhou, J. Biol. Chem., 2013

	G protein	0.86	7.2	**U69.593**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (imaging)	Zhou, J. Biol. Chem., 2013
Isoquinoline 2.2	G protein	1.67	46.7	**U69.593**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (EFC)	Zhou, J. Biol. Chem., 2013
	G protein	2.00	100	**U69.593**	$\Delta\Delta\log(\tau/K_A)$	GTPγS vs β-arrestin-2 (imaging)	Zhou, J. Biol. Chem., 2013
LOR17	G protein	2.931	853	**U50,488**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Bedini, Front. Pharmacol., 2020
Compound 81	G protein	0.78	6	Salvinorin A	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Zheng, J. Med. Chem., 2017

NOR ligand	**Biased pathway**	**Bias factor (β)**	**10^{β} (equation 2)**	**Reference ligand**	**Calculation of bias**	**Assay**	**Reference**
MCOPPB	G protein	1.52	33.1	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-1	Chang, Mol. Pharmacol., 2015
	G protein	1.55	35.5	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	cAMP vs β-arrestin-2	Chang, Mol. Pharmacol., 2015
	G protein	0.97	9.33	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET vs β-arrestin-2	Ferrari, Pharmacol. Res. Pers., 2017
SCH 221510	G protein	0.77	/	**N/OFQ**	$\Delta\log(RA)$	$G_{\beta1}$ BRET vs β-arrestin-2	Malfacini, PloS one, 2015
	G protein	1.10	12.59	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET vs β-arrestin-2	Ferrari, Pharmacol. Res. Pers., 2017
SCH 486757	G protein	0.81	6.46	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET vs β-arrestin-2	Ferrari, Pharmacol. Res. Pers., 2017
UFP-112	G protein	0.71	/	**N/OFQ**	$\Delta\log(RA)$	$G_{\beta1}$ BRET vs β-arrestin-2	Malfacini, PloS one, 2015
PWT2-N/OFQ	G protein	1.09	/	**N/OFQ**	$\Delta\log(RA)$	$G_{\beta1}$ BRET vs β-arrestin-2	Malfacini, PloS one, 2015
Ro65-6570	G protein	1.07	/	**N/OFQ**	$\Delta\log(RA)$	$G_{\beta1}$ BRET vs β-arrestin-2	Malfacini, PloS one, 2015
	G protein	1.00	10	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET vs β-arrestin-2	Ferrari, Eur. J. Pharmacol., 2016
	G protein	1.64	43.65	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET vs β-arrestin-2	Ferrari, Pharmacol. Res. Pers., 2017
Ro2q	G protein	0.93	8.51	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET vs β-arrestin-2	Ferrari, Pharmacol. Res. Pers., 2017
AT-090	β-arrestin	-0.78	0.17	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET vs β-arrestin-2	Ferrari, Eur. J. Pharmacol., 2016
AT-127	G protein	0.27	1.86	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET vs β-arrestin-2	Ferrari, Eur. J. Pharmacol., 2016
AT-202	G protein	0.46	2.88	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET vs β-arrestin-2	Ferrari, Pharmacol. Res. Pers., 2017
AT-403	G protein	0.16	1.45	**N/OFQ**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET vs β-arrestin-2	Ferrari, Pharmacol. Res. Pers., 2017

Bifunctional ligand	**Biased pathway**	**Bias factor (β)**	**10^{β} (equation 2)**	**Reference ligand**	**Calculation of bias**	**Assay (receptor)**	**Reference**
Dmt-c[D-Lys-Phe-Asp]-NH_2	β-arrestin	-1.16	0.07	**EM-2**	$\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET (MOR) vs β-arrestin-2 (MOR)	Gach-Janczak, Peptides, 2018
2*S*-LP2	G protein G protein	0.82 2.31	6.6 204.2	**DADLE** **DADLE**	$\Delta\Delta\log(\tau/K_A)$ $\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET (MOR) vs β-arrestin-2 (MOR) $G_{\beta1}$ BRET (DOR) vs β-arrestin-2 (DOR)	Pasquinucci, Eur. J. Med. Chem., 2019 Pasquinucci, Eur. J. Med. Chem., 2019
***rac*-LP2**	G protein G protein	0.57 2.03	3.7 107.2	**DADLE** **DADLE**	$\Delta\Delta\log(\tau/K_A)$ $\Delta\Delta\log(\tau/K_A)$	$G_{\beta1}$ BRET (MOR) vs β-arrestin-2 (MOR) $G_{\beta1}$ BRET (DOR) vs β-arrestin-2 (DOR)	Pasquinucci, Eur. J. Med. Chem., 2019 Pasquinucci, Eur. J. Med. Chem., 2019