2-(3-Fluoro-4-methylsulfonylaminophenyl) Propanamides as Potent Transient Receptor Potential Vanilloid 1 (TRPV1) Antagonists: Structure Activity Relationships of 2-Amino Derivatives in the *N*-(6-trifluoromethyl-pyridin-3-ylmethyl) C-region

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HPLC Purity and conditions

Columns A: Agilent TC-C18 (5 μm, 4.6 x 250 mm)
B: Agilent Eclipse Plus (5 μm, 4.6 x 250 mm)
C: Daicel Chiralcel OD-H (5 μm, 4.6 x 250 mm)

Conditions :
Flow Rate: 0.8 mL/min, 1.0 mL/min (isocratic)
Wavelength: 254 nm

Compound	Column	Flow rate [mL/min]	Eluent	Retention time [min]	Purity [%]
13	A	0.8	80:20 [a]	6.27	99.34
14	A	0.8	80:20 [a]	7.24	96.48
16	A	1.0	80:20 [a]	5.82	95.86
17	A	0.8	80:20 [a]	6.10	95.90
18	A	0.8	80:20 [a]	6.00	95.75
19	A	0.8	80:20 [a]	7.27	98.97
20	A	0.8	80:20 [a]	7.28	95.54
21	A	0.8	80:20 [a]	6.65	96.43
22	A	0.8	80:20 [a]	5.90	99.27
23	A	0.8	80:20 [a]	6.71	99.01
24	A	0.8	80:20 [a]	3.30	98.78

25	A	0.8	80:20 [a]	3.30	95.39
26	B	0.8	60:40 [c]	5.69	96.42
27	A	0.8	80:20 [a]	7.57	98.23
28	A	0.8	80:20 [a]	7.21	97.69
29	A	0.8	80:20 [a]	6.87	97.71
30	A	0.8	80:20 [a]	6.15	97.84
31	A	0.8	80:20 [a]	6.15	97.84
32	A	0.8	80:20 [a]	5.50	95.10
33	A	0.8	80:20 [a]	5.30	98.85
34	C	1.0	80:20 [d]	11.42, 14.58	98.40
35	C	1.0	80:20 [d]	14.59	95.76
36	C	1.0	80:20 [d]	13.49	95.44
37	C	1.0	80:20 [d]	10.86	96.61
38	C	1.0	60:40 [g]	7.40	96.64
39	C	1.0	80:20 [d]	22.72	96.64
40	C	1.0	70:30 [e]	11.39	95.17
41	C	1.0	50:50 [e]	9.72	95.87
42	C	1.0	60:40 [g]	7.53	96.84
43	C	1.0	60:40 [f]	7.29	96.68
44	A	0.8	80:20 [a]	6.07	95.27
45	A	0.8	80:20 [a]	5.68	96.85
45S	C	1.0	80:20 [d]	9.34	96.21
46	A	0.8	80:20 [a]	5.45	96.53

47	A	1.0	80:20 [a]	3.67	95.31
48	A	1.0	80:20 [a]	5.03	99.55
49	A	0.8	80:20 [a]	6.38	99.01
49S	C	1.0	80:20 [h]	9.94	96.68
49R	C	1.0	80:20 [h]	8.23	95.16
50	A	0.8	80:20 [a]	7.32	99.26
51	A	0.8	80:20 [a]	6.98	99.55
52	A	0.8	80:20 [a]	7.33	97.99
53	A	0.8	80:20 [a]	7.26	98.69
54	B	0.8	70:30 [b]	36.93	95.73
55	A	0.8	80:20 [a]	7.21	97.28
56	A	0.8	80:20 [a]	7.05	95.97
57	A	0.8	80:20 [a]	8.05	99.56
58	A	0.8	80:20 [a]	9.60	99.39
59	A	0.8	80:20 [a]	8.09	97.31
60	A	0.8	80:20 [a]	8.18	95.82
61	A	0.8	80:20 [a]	5.12	95.90
62	A	0.8	80:20 [a]	5.09	95.06
63	A	0.8	80:20 [a]	5.89	96.46
64	A	0.8	80:20 [a]	4.44	96.97
65	A	0.8	80:20 [a]	4.15	99.43
66	A	0.8	80:20 [a]	4.99	99.10
67	A	0.8	80:20 [a]	5.47	99.27

68	A	0.8	80:20 [a]	5.40	99.25
69	A	0.8	80:20 [a]	7.25	99.09
70	A	0.8	80:20 [a]	5.95	99.25
71	A	1.0	80:20 [a]	4.02	99.80
72	A	0.8	80:20 [a]	6.86	99.38
73	A	0.8	80:20 [a]	5.09	95.14
74	B	0.8	80:20 [a]	3.09	95.51
75	A	0.8	80:20 [a]	5.69	97.12
76	A	0.8	80:20 [a]	5.91	96.59
79	A	0.8	80:20 [a]	6.36	99.67
80	A	0.8	80:20 [a]	7.11	99.39
81	A	0.8	80:20 [a]	3.47	95.53
82	B	0.8	90:10 [a]	2.73	98.29
83	A	0.8	80:20 [a]	3.30	95.17
84	A	0.8	80:20 [a]	4.81	98.62
85	A	0.8	80:20 [a]	4.79	99.24
86	A	0.8	80:20 [a]	4.35	98.73
87	A	0.8	80:20 [a]	6.29	98.52
88	A	0.8	80:20 [a]	5.20	99.68
89	B	0.8	80:20 [a]	6.47	95.27
90	A	0.8	80:20 [a]	3.68	96.63
92	B	0.8	90:10 [a]	2.73	99.25
95	A	0.8	80:20 [a]	6.58	96.88

96	A	0.8	80:20 [a]	3.31	97.42
97	A	1.0	80:20 [a]	3.71	99.02
98	C	1.0	80:20 [b]	8.54, 9.90	98.50
99	A	0.8	80:20 [a]	4.18	95.20

[a] Acetonitrile:H_2O containing 0.1% TFA, [b] MeOH:H_2O containing 0.1% TFA, [c] MeOH:H_2O containing 4mM NH_3, [d] n-Hexane:2-PrOH containing 0.1% TFA, [e] n-Hexane:2-PrOH, [f] n-Heptane:2-PrOH containing 0.1% TFA, [g] n-Heptane:2-PrOH containing 4mM NH_3, [h] n-Heptane:2-PrOH.