Electronic Supplementary Information (ESI)

Title:

Bioisosteric Replacement of the Pyrazole 3-Carboxamide Moiety of Rimonabant. A Novel Series of Oxadiazoles as CB1 Cannabinoid Receptor Antagonists

Author:

Cheng-Ming Chu, Ming-Shiu Hung, Min-Tsang Hsieh, Chun-Wei Kuo, Suja T. D., Jen-Shin Song, Hua-Hao Chiu, Yu-Sheng Chao and Kak-Shan Shia*

Division of Biotechnology and Pharmaceutical Research, National Health Research Institutes, Miaoli County 350, Taiwan, R.O.C. *E-mail:* ksshia@nhri.org.tw

*To whom correspondence should be addressed.

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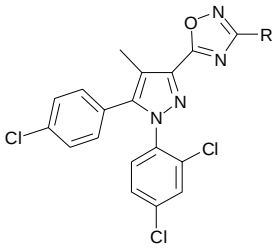
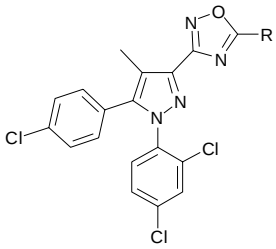
Table 2 Biological evaluation of 3-alkyloxadiazoles and 5-alkyloxadiazoles on hCB1and hCB2 receptors (Ki)



4a-k



8a-h

Compd	R	hCB1[a, b] Ki(nM)	hCB2[a, b] Ki(nM)
4a	CH_3	271.3 ± 5.9	>5000
4b	CH_2CH_3	119.8 ± 23.9	2713.5 ± 212.6
4c	$CH_2CH_2CH_3$	155.0 ± 46.6	3134.9 ± 436.6
4d	$CH_2(CH_2)_2CH_3$	136.2 ± 7.3	>5000
4e	$CH_2(CH_2)_3CH_3$	117.5 ± 14.9	>5000
4f	$CH(CH_3)_2$	42.7 ± 10.4	2887.5 ± 302.3
4g	$CH(C_2H_5)_2$	33.1 ± 7.8	1455.6 ± 531.2
4h	$C(CH_3)_3$	34.4 ± 4.6	2167.7 ± 39.8
4i	*c*-C_3H_5	61.0 ± 5.0	2833.2 ± 51.0
4j	$CH_2CH(CH_3)_2$	161.9 ± 4.9	3839.1 ± 377.6
4k	CH_2(*c*-C_3H_5)	231.7 ± 108.7	4139.2 ± 343.9
8a	CH_3	492.4 ± 56.3	>5000
8b	CH_2CH_3	144.1 ± 25.3	>5000
8c	$CH_2CH_2CH_3$	85.3 ± 21.8	4155.4 ± 166.1
8d	$CH(CH_3)_2$	41.4 ± 12.8	3761.8 ± 549.1
8e	$CH(C_2H_5)_2$	29.3 ± 9.4	554.4 ± 70.2
8f	$C(CH_3)_3$	16.2 ± 4.6	4082.5 ± 112.0
8g	CF_3	19.8 ± 2.7	>5000
8h	$C(CH_3)_2CF_3$	7.6 ± 2.1	1478.0 ± 573.1
	SR141716A	7.6 ± 0.5	685.4 ± 44.6

[a]Data are expressed as the mean ± SD of at least three independent experiments.

[b]Binding affinity determined by inhibition of [^{3}H]-CP55940 binding to the membrane of hCB1 or hCB2-expressing HEK 293 cells is expressed as Ki.