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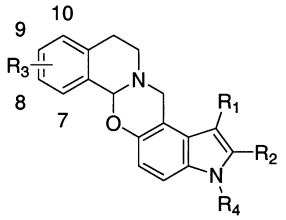
Thomas M. Böhme,* Corinne E. Augelli-Szafran, Hussein Hallak, Thomas Pugsley, Kevin Serpa, and Roy D. Schwarz: Synthesis and Pharmacology of Benzoxazines as Highly Selective Antagonists at M_4 Muscarinic Receptors.

Page 3096. Entries in the first column of Table 1 are missing. The correct table is shown below.

Table 1. Binding Results of Benzoxazines



					pK_i [a]						
example	R^1	R^2	R^3	R^4	M_1	M_2	M_3	M_4	M_5	formula[c]	mp (°C)
16	CO_2CH_3	CH_3	9-OMe	CH_3	5.93	6.38	6.40	6.72	5.44	$C_{23}H_{24}N_2O_4$	194−195
17	$CO_2CH_2CH{=}CH_2$	CH_3	9-OMe	H	5.88	5.97	6.39	7.82	5.65	$C_{24}H_{24}N_2O_4{\cdot}0.1H_2O$	188−190
18	$CO_2CH_2CH{=}CH_2$	CH_3	9-OMe	(*p*-OMe)Bz	6.70	6.62	6.17	7.14	6.30	$C_{32}H_{32}N_2O_5{\cdot}0.04H_2O$	175−176
19	$CO_2CH_2C_6H^{15}$	CH_3	9-OMe	H	5.93	5.87	5.86	7.14	5.95	$C_{28}H_{26}N_2O_4$	176−178
20	$CO_2(CH_2)3CH_3$	CH_3	9-OMe	H	5.88	5.63	5.99	7.17	5.60	$C_{25}H_{28}N_2O_4$	177−178
21	$CO_2CH_2CH_3$	CH_2CH_3	9-OMe	H	5.66	5.87	7.04	8.40	5.51	$C_{24}H_{26}N_2O_4$	183−184
22	$CO_2CH_2CH_3$	CH_2CH_3	9-OMe	benzyl	6.44	6.43	7.30	7.01	6.32	$C_{31}H_{32}N_2O_4{\cdot}0.04H_2O$	75−85
23	$CO_2CH_2CH_3$	CH_2CH_3	9-OMe	CH_3	5.82	6.15	6.66	8.52	5.51	$C_{25}H_{28}N_2O_4{\cdot}0.06H_2O$	172−174
24	**$CO_2CH_2CH_3$**	**$(CH_2)_2CH_3$**	**9-OMe**	**H**	**5.69**	**5.97**	**7.15**	**8.70**	**5.65**	**$C2sHN_2O_4{\cdot}0.11H_2O$**	**194−196**
25	$CO_2CH_2CH_3$	$(CH_2)_2CH_3$	9-SMe	H	6.06	5.84	7.00	9.00	5.62	$C_{25}H_{28}N_2O_3S{\cdot}0.02H_2O$	185−186
26	$CO_2CH_2CH_3$	$(CH_2)_2CH_3$	9-SMe	CH_3	5.48	5.42	6.64	8.70	5.77	$C_{26}H_{30}N_2O_3S{\cdot}0.27H_2O$	139−143
27	$CO_2CH_2CH_3$	$(CH_2)_2CH_3$	9-OMe	CH_3	5.88	6.29	7.15	8.70	5.47	$C_{26}H_{30}N_2O_4$	150−151
28	**$CO_2CH_2CH_3$**	**$(CH_2)_3CH_3$**	**9-OMe**	**H**	**4.88**	**6.47**	**6.82**	**9.00**	**4.95**	**$C_{26}H_{30}N_2O_4$**	**180−182**
29	$CO_2CH_2CH_3$	$(CH_2)_3CH_3$	9-SMe	H	6.06	5.66	6.47	8.52	5.83	$C_{26}H_{30}N_2O_3S$	159−161
30	$CO_2CH_2CH_3$	$(CH_2)_4CH_3$	9-OMe	H	4.69	5.14	6.34	7.96	5.27	$C_{27}H_{32}N_2O_4$	170−172
31	$CO_2CH_2CH_3$	$(CH_2)_5CH_3$	9-OMe	H	5.51	5.34	6.55	7.85	>4.55	$C_{28}H_{34}N_2O_4$	157−160
32	$CO_2CH_2CH_3$	CH_3	9-C1	H	5.29	5.49	5.56	6.44	5.27	$C_{22}H_{21}ClN_2O_3{\cdot}0.7H_2O$	196−197
33	$CO_2CH_2CH_3$	CH_3	7-C1	H	>5.36	5.61	5.29	5.71	5.32	$C_{22}H_{21}CIN_2O_3$[d]	188−189
34	$CO_2CH_2CH_3$	CH_3	9-SMe	H	5.75	5.66	6.64	8.15	5.71	$C_{23}H_{24}N_2O_3S{\cdot}0.02H_2O$	188−189
35	$CO_2CH_2CH_3$	CH_3	9-OH	H	>4.66	>4.57	4.59	>4.91	>4.55	$C_{22}H_{22}N_2O_4$[e]	241−243
36	$CO_2CH_2CH_3$	CH_3	9-OMe	CH_2CH_3	5.88	6.66	6.58	6.96	5.60	$C_{25}H_{28}N_2O_4$[f]	173−175
37	$CO_2CH_2CH_3$	CH_3	9-OMe	CH_3	5.70	6.29	6.04	7.82	5.43	$C_{24}H_{26}N_2O_4{\cdot}0.1H_2O$	174−176
38	$CONCH_3C_2H_5$	CH_3	9-OMe	H	4.66	5.39	4.81	5.01	4.71	$C_{24}H_{27}N_3O3$[g]	162−164
39	$CH_2C_5H_6$	CH_3	9-OMe	H	5.60	5.27	5.69	5.87	5.95	$C_{27}H_{26}N_2O_2{\cdot}0.04H_2O$	196−198
40	oxadiazole[b]	CH_3	9-OMe	H	5.12	5.66	5.51	7.21	5.21	$C_{23}H_{22}N_4O_3{\cdot}0.19H_2O$	195−197
41 (PD102807)	$CO_2CH_2CH_3$	CH_3	9-OMe	H	5.88	6.27	6.59	8.15	5.47	$C_{23}H_{24}N_2O_4$	190−192

[a] The affinity of these compounds for the five human receptor subtypes (M_1−M_5) was determined by [^{3}H]-NMS binding using membranes from transfected Chinese hamster ovarian (CHO) cells. All compounds were tested at least three times, and the value shown is given as the geometric mean. The standard error of the mean (SEM) for all compounds tested ranged from 6% to 18%. The complete protocol is described by Dörje et al.[12] and Buckley et al.[13] The K_i values of the test compounds were derived from IC_{50} values using the Cheng−Prusoff equation, $K_i - IC_{50}/(1 + L/K_d)$, with the radioligand concentration $L = 0.1$ nM and the following equilibrium dissociation constants K_D of [_H] NMS, determined in previous saturation binding experiments (nM): M_1 (1.28); M_2 (0.85); M_3 (0.94); M_4 (3.10); M_5 (0.79).[30] [b] Oxadiazole = 3-methyl[1,2,4]oxadiazol-5-yl. [c] All compounds have analytical results within ±0.4% of theoretical values unless otherwise noted. Some difficulty was found in obtaining combustion analysis in the indicated compounds because of the propensity of these compounds to retain solvents. [d] High mass: calcd 397.1319; found 397.1325. [e] High mass: calcd 379.1658; found 379.1651. [f] High mass: calcd 421.2127; found 421.2122. [g] High mass: calcd 406.2130; found 406.2137.

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