Supporting Information

Methyl Substitution on the Piperidine Ring of *N*-[ω-(6-Methoxynaphthalen-1-yl)alkyl] Derivatives as a Probe for Selective Binding and Activity at the σ_1 Receptor

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Elemental analyses of the end products;

^{1}H NMR and GC-MS data for the products **10a,b**, **17**, **18**, **20**, **29**–**34**;

$[\alpha]_D$ data for the enantiomeric couples **29** and **30**.

Elemental Analyses

	Calculated			Found		
Compound	**C**	**H**	**N**	**C**	**H**	**N**
11	68.55	9.39	4.21	68.65	9.26	4.44
12	71.09	9.54	4.14	70.70	9.55	4.22
13	69.88	9.77	3.88	69.60	9.43	4.03
15	69.88	9.77	3.88	69.57	9.45	3.90
16	71.09	9.54	4.14	71.06	9.51	4.43
17	71.66	9.74	3.98	71.69	10.16	3.84
18	70.47	9.95	3.74	70.07	9.67	3.82
20	70.47	9.95	3.74	70.76	9.61	3.83
21	71.34	8.19	4.38	71.09	8.58	4.51
(–)-(*R*)-**22**	71.94	8.45	4.19	71.87	8.85	4.39
(+)-(*S*)-**22**	71.94	8.45	4.19	72.20	8.86	4.26
(–)-(*R*)-**23**	71.94	8.45	4.19	71.55	8.53	4.51
(+)-(*S*)-**23**	71.94	8.45	4.19	72.20	8.68	4.33
24	70.24	8.52	4.10	70.56	8.76	4.18
25	70.67	8.75	3.92	70.65	8.47	4.04
26	71.57	8.72	3.97	71.80	8.67	3.64
27	71.57	8.72	3.97	71.67	9.16	4.07
28	71.94	8.45	4.19	72.04	8.66	4.39
(–)-(*R*)-**29**	70.67	8.75	3.92	70.50	8.90	3.99
(+)-(*S*)-**29**	72.50	8.69	4.03	72.24	8.65	4.23
(–)-(*R*)-**30**	72.50	8.69	4.03	72.36	9.24	4.01
(+)-(*S*)-**30**	72.50	8.69	4.03	72.73	9.16	4.38
31	72.50	8.69	4.03	72.27	9.11	4.05
32	71.23	8.97	3.78	70.94	8.68	3.86
33	73.00	8.91	3.87	73.30	9.04	4.00
34	71.23	8.97	3.78	70.83	9.41	3.85

^{1}H NMR, GC-MS and $[\alpha]_D$ data

1-(3-Bromopropyl)-6-methoxynaphthalene (10a). ^{1}H-NMR: δ 2.20-2.38 (m, 2H, C*H*$_2$CH$_2$Br), 3.20 (t, 2H, *J* = 7.5 Hz, benzyl CH$_2$), 3.44 (t, 2H, *J* = 6.4 Hz, CH$_2$Br), 3.92 (s, 3H, OCH$_3$), 7.12-7.95 (m, 6H, aromatic); GC-MS *m/z* 280 (M^++2, 52), 279 (M^+ +1, 8), 278 (M^+, 53), 171 (100), 128 (25).

1-(4-Chlorobutyl)-6-methoxynaphthalene (10b). ^{1}H-NMR (90 MHz): δ 1.75-1.98 [m, 4H, (C*H*$_2$)$_2$CH$_2$Cl], 2.90-3.30 (m, 2H, benzyl CH$_2$), 3.55-3.75 (m, 2H, CH$_2$Cl), 3.92 (s, 3H, OCH$_3$), 7.10-8.10 (m, 6H, aromatic); GC-MS *m/z* 250 (M^++2, 33), 249 (M^+ +1, 17), 248 (M^+, 78), 171 (100), 128 (34).

4-Methyl-1-[4-(6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)butyl]piperidine (17). ^{1}H NMR: δ 0.91 (d, 3H, *J* = 6 Hz, CHC*H*$_3$), 1.38-1.45 [m, 5H, CH$_3$C*H*(C*H*$_2$)$_2$], 1.51-1.85 [m, 10H, (C*H*$_2$)$_2$CH(C*H*$_2$)$_3$], 1.92-2.05 [m, 2H, (CH$_2$)$_3$C*H*$_2$N], 2.35 [t, 2H, *J* = 8.3 Hz, N(C*H*H)$_2$], 2.63-2.75 (m, 3H, benzyl CH and CH$_2$), 2.91-3.04 [m, 2H, N(CH*H*)$_2$], 3.75 (s, 3H, OCH$_3$), 6.58-7.08 (m, 3H, aromatic); GC-MS *m/z* 316 (M^++1, 15), 315 (M^+, 53), 112 (100). Anal. ($C_{21}H_{33}NO{\cdot}HCl$) C, H, N.

2,2-Dimethyl-1-[3-(6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)butyl]piperidine (18). ^{1}H NMR: δ 1.01 [s, 6H, C(CH$_3$)$_2$], 1.20-1.95 [m, 16H, C(CH$_2$)$_3$ and (C*H*$_2$)$_2$CH(C*H*$_2$)$_3$], 2.25-2.58 (m, 4H, CH$_2$NCH$_2$), 2.62-2.78 (m, 3H, benzyl CH and CH$_2$), 3.78 (s, 3H, OCH$_3$), 6.58-7.15 (m, 3H, aromatic); GC-MS *m/z* 330 (M^++1, 4), 329 (M^+, 18), 314 (100), 126 (48). Anal. ($C_{22}H_{35}NO{\cdot}HCl{\cdot}{}^1/_2H_2O$) C, H, N.

4,4-Dimethyl-1-[4-(6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)butyl]piperidine (20). ^{1}H NMR: δ 0.99 [s, 6H, C(CH$_3$)$_2$], 1.35-1.98 [m, 14H, CH$_2$CCH$_2$ and (C*H*$_2$)$_2$CH(C*H*$_2$)$_3$], 2.38-2.45 [m, 6H, CH$_2$N(CH$_2$)$_2$], 2.78-2.85 (m, 3H, benzyl CH and CH$_2$), 3.85 (s, 3H, OCH$_3$),

6.60-7.15 (m, 3H, aromatic); GC-MS *m/z* 330 (M^++1, 2), 329 (M^+, 11), 126 (100). Anal. ($C_{22}H_{35}NO{\cdot}HCl{\cdot}^1/_2H_2O$) C, H, N.

(–)-(*R*)-2-Methyl-1-[4-(6-methoxynaphthalen-1-yl)butyl]piperidine [(–)-(*R*)-29]. $[\alpha]_D$ = – 4.8° (c = 1%, MeOH); ^{1}H NMR: δ 1.10 (d, 3H, *J* = 6 Hz, CHC*H*$_3$), 1.20-1.38 (m, 2H, CHCH$_2$C*H*$_2$), 1.48-1.78 [m, 8H, CHC*H*$_2$CH$_2$C*H*$_2$ and ArCH$_2$(C*H*$_2$)$_2$], 2.08-2.42 [m, 3H, Ar(CH$_2$)$_3$C*H*$_2$ and C*H*CH$_3$], 2.67-2.77 (m, 1H, NC*H*H), 2.82-2.87 (m, 1H, NCH*H*), 3.05 (t, 2H, *J* = 7.5 Hz, benzyl CH$_2$), 3.92 (s, 3H, OCH$_3$), 7.14-7.97 (m, 6H, aromatic); GC-MS *m/z* 312 (M^++1, 4), 311 (M^+, 17), 296 (41), 112 (100). Anal. ($C_{21}H_{29}NO{\cdot}HCl{\cdot}^1/_2H_2O$) C, H, N.

(+)-(*S*)-2-Methyl-1-[4-(6-methoxynaphthalen-1-yl)butyl]piperidine [(+)-(*S*)-29]. $[\alpha]_D$ = + 4.9° (c = 1%, MeOH). Anal. ($C_{21}H_{29}NO{\cdot}HCl$) C, H, N.

(–)-(*R*)-3-Methyl-1-[4-(6-methoxynaphthalen-1-yl)butyl]piperidine [(–)-(*R*)-30]. $[\alpha]_D$ = – 4.4° (c = 1%, MeOH); ^{1}H NMR: δ 0.79-0.96 (m, 4H, CHCH$_3$), 1.48-1.80 [m, 10H, CH(C*H*$_2$)$_2$ and ArCH$_2$(C*H*$_2$)$_3$], 2.28-2.40 [m, 2H, N(C*H*H)$_2$], 2.80-2.98 [m, 2H, N(CH*H*)$_2$], 3.01-3.06 (m, 2H, benzyl CH$_2$), 3.92 (s, 3H, OCH$_3$), 7.14-8.01 (m, 6H, aromatic); GC-MS *m/z* 312 (M^++1, 5), 311 (M^+, 21), 112 (100). Anal. ($C_{21}H_{29}NO{\cdot}HCl$) C, H, N.

(+)-(*S*)-3-Methyl-1-[4-(6-methoxynaphthalen-1-yl)butyl]piperidine [(+)-(*S*)-30]. $[\alpha]_D$ = + 4.3° (c = 1%, MeOH). Anal. ($C_{21}H_{29}NO{\cdot}HCl$) C, H, N.

4-Methyl-1-[4-(6-methoxynaphthalen-1-yl)butyl]piperidine (31). ^{1}H NMR: δ 0.92 (d, 3H, *J* = 6 Hz, CHC*H*$_3$), 1.20-1.40 [m, 3H, C*H*(C*H*H)$_2$], 1.56-1.78 [m, 6H, CH(CH*H*)$_2$ and ArCH$_2$(C*H*$_2$)$_2$], 1.81-1.92 [m, 2H, Ar(CH$_2$)$_3$C*H*$_2$], 2.30-2.38 [m, 2H, N(CH*H*)$_2$], 2.80-2.92 [m, 2H, N(C*H*H)$_2$], 3.05 (t, 2H, *J* = 7.5 Hz, benzyl CH$_2$), 3.95 (s, 3H, OCH$_3$), 7.18-7.98 (m, 6H, aromatic); GC-MS *m/z* 312 (M^++1, 4), 311 (M^+, 17), 112 (100). Anal. ($C_{21}H_{29}NO{\cdot}HCl$) C, H, N.

2,2-Dimethyl-1-[3-(6-methoxynaphthalen-1-yl)butyl]piperidine (32). ^{1}H NMR: δ 1.00 [s, 6H, $C(CH_3)_2$], 1.38-1.80 [m, 10H, $C(CH_2)_3$ and $ArCH_2(CH_2)_2$], 2.30-2.51 (m, 4H, CH_2NCH_2), 3.08 (t, 2H, J = 7.5 Hz, benzyl CH_2), 3.95 (s, 3H, OCH_3), 7.12-8.02 (m, 6H, aromatic); GC-MS *m/z* 326 (M^++1, 5), 325 (M^+, 20), 310 (100), 126 (40). Anal. ($C_{22}H_{31}NO{\cdot}HCl{\cdot}{}^1/_2H_2O$) C, H, N.

3,3-Dimethyl-1-[4-(6-methoxynaphthalen-1-yl)butyl]piperidine (33). ^{1}H NMR: δ 0.95 [s, 6H, $C(CH_3)_2$], 1.18-1.35 (m, 4H, CCH_2CH_2), 1.62-1.81 [m, 4H, $ArCH_2(CH_2)_2$], 1.99 (br s, 2H, NCH_2C), 2.22-2.38 (m, 4H, CH_2NCH_2), 3.03 (t, 2H, J = 7.5 Hz, benzyl CH_2), 3.95 (s, 3H, OCH_3), 7.18-7.99 (m, 6H, aromatic); GC-MS *m/z* 326 (M^++1, 10), 325 (M^+, 36), 171 (21), 126 (100). Anal. ($C_{22}H_{31}NO{\cdot}HCl$) C, H, N.

4,4-Dimethyl-1-[4-(6-methoxynaphthalen-1-yl)butyl]piperidine (34). ^{1}H NMR: δ 0.91 [s, 6H, $C(CH_3)_2$], 1.38-1.44 (m, 4H, CH_2CCH_2), 1.58-1.78 [m, 4H, $ArCH_2(CH_2)_2$], 2.35-2.44 [m, 6H, $CH_2N(CH_2)_2$], 3.01-3.06 (m, 2H, benzyl CH_2), 3.92 (s, 3H, OCH_3), 7.14-7.97 (m, 6H, aromatic); GC-MS *m/z* 326 (M^++1, 4), 325 (M^+, 18), 126 (100). Anal. ($C_{22}H_{31}NO{\cdot}HCl{\cdot}{}^1/_2H_2O$) C, H, N.