SUPPLEMENTARY INFORMATON

Optimization of a Series of Mu Opioid Receptor (MOR) Agonists with High G Protein Signaling Bias

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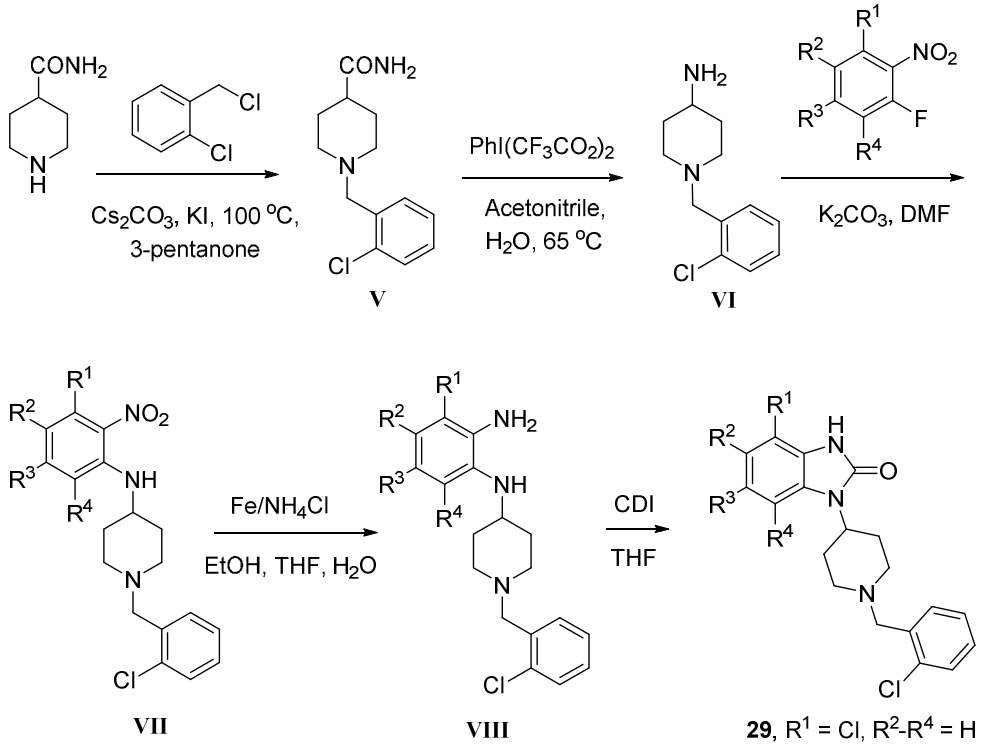
Table of Contents

Scheme S1. Synthetic route for the preparation of 4-chloro-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one (**29**) from isonipecotamide.



1-(2-Chlorobenzyl)piperidin-4-one, (**V**)[1]

A mixture of isonipecotamide (5.0 g, 39 mmol), Cs_2CO_3 (8.0 g, 24 mmol), potassium iodide (650 mg, 3.9 mmol), 3-pentanone (25 mL), and 2-chlorobenzyl chloride (6.1 mL, 47 mmol) was stirred for 5 h at 100 °C. The mixture was filtered hot and the filtercake was washed with acetone. The filtrate was concentrated and the resulting slurry was recrystallized in acetone to afford pure product **V** (7.2 g, 73% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.2 Hz, 1H), 7.33 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.23 (td, *J* = 6.8, 1.4 Hz, 1H), 7.17 (td, *J* = 7.6, 2.0 Hz, 1H), 5.59 (d, *J* = 41.2 Hz, 2H), 3.61 (s, 2H), 2.96 (dd, *J* = 8.8, 2.8 Hz, 2H), 2.21-2.10 (m, 2H), 1.87 (d, *J* = 10.8 Hz, 2H), 1.78 (qd, *J* = 12.4, 3.6 Hz, 2H); MS(*m/z*): [M + H] calc'd for $C_{13}H_{18}ClN_2O$ is 253.10, found 253.06.

***N*-(3-chloro-2-nitrophenyl)-1-(2-chlorobenzyl)piperidin-4-amine**, (**VII**)

A mixture of bis(trifluoroacetoxy)iodobenzene (3.6 g, 8.4 mmol), **V** (2.0 g, 7.9 mmol), acetonitrile (20 mL), and water (15 mL) was heated at 65 ^{o}C overnight. Upon completion, the reaction mixture was quenched with $HCl_{(aq)}$ and extracted with diethyl ether. The aqueous layer was then saturated with K_2CO_3 and extracted with CH_2Cl_2; the combined organic layers were dried over Na_2SO_4 and concentrated to dryness. The crude product, 1-(2-chlorobenzyl)piperidin-4-amine (**VI**), was used without further purification (1.6 g). MS(*m/z*): [M + H] calc'd for $C_{12}H_{18}ClN_2$ is 225.11, found 224.89.

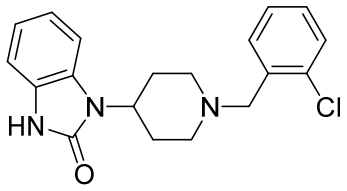
A mixture of **VI** (266 mg, 1.2 mmol), 2-chloro-6-fluoronitrobenzene (176 mg, 1.0 mmol), K_2CO_3 (276 mg, 2.0 mmol), and DMF (5 mL) was stirred at room temperature overnight under argon. The reaction mixture was quenched with water and the aqueous layer was extracted with CH_2Cl_2; the combined organic layers were dried over Na_2SO_4 and concentrated to dryness. Purification via silica gel chromatography afforded pure product **VII** (392 mg, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 6.0 Hz, 1H), 7.36 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.27-7.17 (m, 3H), 6.72 (dd, *J* = 6.4, 3.2 Hz, 1H), 5.76 (d, *J* =6.8 Hz, 1H), 3.66 (s, 2H), 3.44-3.42 (m, 1H), 2.87 (d, *J* = 10.8 Hz, 2H), 2.32 (t, *J* = 10.8 Hz, 2H), 2.03 (d, *J* = 10.4 Hz, 2H), 1.64-1.57 (m, 2H); MS(*m/z*): [M + H] calc'd for $C_{18}H_{20}Cl_2N_3O_2$ is 380.09, found 379.09.

3-Chloro-N^1-(1-(2-chlorobenzyl)piperidin-4-yl)benzene-1,2-diamine, (**VIII**)

A mixture of **VII** (114 mg, 0.3 mmol), ammonium chloride (16 mg, 0.3 mmol), iron powder (134 mg, 2.4 mmol), EtOH (3 mL), THF (1 mL), and water (0.5 mL) was stirred at 100 ^{o}C for 3 h. and

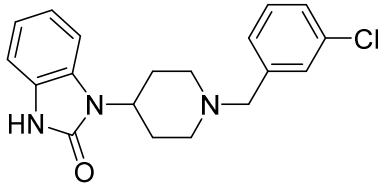
then filtered through a pad of Celite®. The pad was washed with MeOH and the filtrate was concentrated to dryness. Purification via silica gel chromatography afforded pure product **VIII** (70 mg, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (t, *J* = 5.6 Hz, 1H), 7.35 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.25 (td, *J* = 7.4, 1.2 Hz, 1H), 7.20 (td, *J* = 7.4, 2.0 Hz, 1H), 6.82-6.65 (m, 3H), 6.57 (dd, *J* = 7.8, 1.0 Hz, 1H), 3.66 (d, *J* = 2.4 Hz, 2H), 3.29 (tt, *J* = 12.8, 4.0 Hz, 1H), 2.91 (d, *J* = 10.0 Hz, 2H), 2.30 (t, *J* = 10.2 Hz, 2H), 2.08-2.04 (m, 2H), 1.57 (dd, *J* = 12.4, 10.4 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{18}H_{22}Cl_2N_3$ is 350.11, found 348.11.

1-(1-(2-Chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**2**)



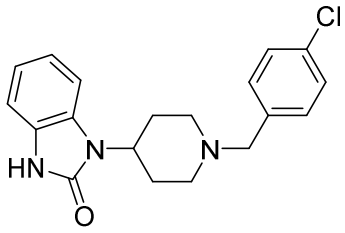
A mixture of 1-(piperidin-4-yl)-1H-benzo[d]imidazol-2(3H)-one (free base, 110 mg, 0.5 mmol), 2-chlorobenzaldehyde (0.2 g, 1.4 mmol), AcOH (drops), $NaBH(OAc)_3$ (0.3 g, 1.4 mmol), and DCE (5 mL) was stirred at room temperature overnight under argon. The reaction mixture was quenched with saturated $NaHCO_3$ and then extracted with CH_2Cl_2; the combined organic layers were dried over Na_2SO_4 and concentrated to dryness. Purification via silica gel chromatography afforded pure product **2** (78 mg, 45% yield). ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.83 (s, 1H), 7.58 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.44 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.38-7.34 (m, 2H), 7.32-7.22 (m, 1H), 6.99-6.96 (m, 3H), 4.17 (tt, *J* = 12.2, 4.2 Hz, 1H), 3.63 (s, 2H), 2.97 (d, *J* = 11.6 Hz, 2H), 2.38 (qd, *J* = 12.2, 3.6 Hz, 2H), 2.22 (t, *J* = 11.0 Hz, 2H), 1.65 (dd, *J* = 12.0, 2.4 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{21}ClN_3O$ is 342.13, found 342.10; HPLC t_R = 3.57 min.

1-(1-(3-Chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**3**)



This compound was preared according to the procedure for compound **2** in 29% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 8.02 (s, 1H), 7.39-7.26 (m, 3H), 7.09-7.04 (m, 4H), 4.44-4.35 (m, 1H), 3.54 (s, 2H), 3.02 (d, *J* = 11.2 Hz, 2H), 2.48 (q, *J* = 8.8 Hz, 2H), 2.18 (t, *J* = 11.4 Hz, 2H), 1.80 (d, *J* = 11.2 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{21}ClN_3O$ is 342.13, found 342.15; HPLC t_R = 3.62 min.

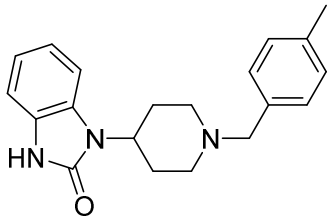
1-(1-(4-Chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**4**)[2]



A mixture of 1-(piperidin-4-yl)-1H-benzo[d]imidazol-2(3H)-one (20 mg, 0.06 mmol), 4-chlorobenzyl bromide (12 mg, 0.06 mmol), K_2CO_3 (28 mg, 0.2 mmol), NaI (9.0 mg, 0.06 mmol), and DMF (0.6 mL) was stirred at 90 ^{o}C for 24 h under argon. The reaction mixture was quenched with water and then extracted with EtOAc; the combined organic layers were dried over Na_2SO_4 and concentrated to dryness. Purification via silica gel chromatography afforded pure product **4** (8.0 mg, 39% yield), which was dissolved in a solution of methane sulfonic acid in EtOH (0.06 M, 0.4 mL, 0.02 mmol). The solvent was removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was frozen and then subjected to lyophilization overnight giving product **4** in the form of a mesylate salt. ^{1}H

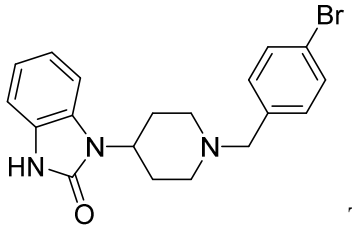
NMR mesylate (400 MHz, CD_3OD) δ 7.56-7.54 (m, 4H), 7.29-7.26 (m, 1H), 7.10-7.07 (m, 3H), 4.56 (tt, *J* = 12.4, 4.0 Hz, 1H), 4.39 (s, 2H), 3.66 (dd, *J* = 10.6, 1.8 Hz, 2H), 3.27-3.23 (m, 2H), 2.80 (qd, *J* = 13.4, 3.8 Hz, 2H), 2.72 (s, 3H), 2.09 (d, *J* = 14.8 Hz, 2H); MS(*m/z*): [M + H] calc'd for $C_{19}H_{20}ClN_3O$ is 341.84, found 342.02; HPLC t_R = 3.67 min.

1-(1-(4-Methylbenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**5**)



This compound was prepared according to the procedure for compound **2** in 59% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.31-7.28 (m, 3H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.11-7.04 (m, 3H), 4.38 (tt, *J* = 12.6, 3.8 Hz, 1H), 3.58 (s, 2H), 3.08 (d, *J* = 10.0 Hz, 2H), 2.53-2.51 (m, 2H), 2.35 (s, 3H), 2.20 (t, *J* = 10.8 Hz, 2H), 1.81 (dd, *J* = 12.0, 2.0 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{24}N_3O$ is 322.18, found 322.03; HPLC t_R = 3.59 min.

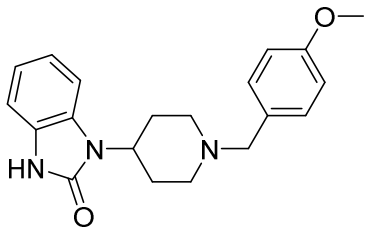
1-(1-(4-Bromobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**6**)



This compound was prepared according to the procedure for compound **2** in 56% yield. Methane sulfonic acid (17 μL, 0.3 mmol) was added to a suspension of the product in EtOH (1 mL). The mixture was heated to 60 ^{o}C for 30 min. The solvent was

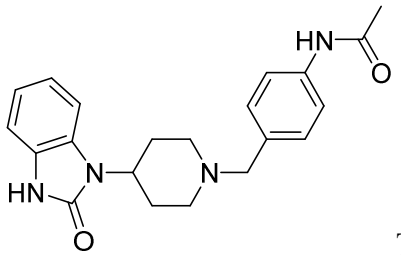
removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was frozen and then subjected to lyophilization overnight giving product **6** in the form of a mesylate salt. ^{1}H NMR mesylate (400 MHz, CD_3OD) δ 7.71 (dd, *J* = 6.4, 2.0 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.27-7.25 (m, 1H), 7.10-7.07 (m, 3H), 4.55 (tt, *J* = 12.2, 4.4 Hz, 1H), 4.37 (s, 2H), 3.66 (d, *J* = 12.4 Hz, 2H), 3.26-3.24 (m, 2H), 2.80 (qd, *J* = 13.4, 3.6 Hz, 2H), 2.72 (s, 3H), 2.08 (d, *J* = 12.8 Hz, 2H); MS(*m/z*): [M + H] calc'd for $C_{19}H_{21}BrN_3O$ is 386.08, found 386.01; HPLC t_R = 3.72 min.

1-(1-(4-Methoxybenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**7**)[3]



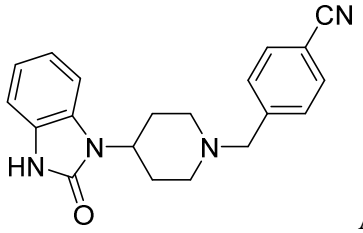
This compound was prepared according to the procedure for compound **2** in 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.30-7.28 (m, 3H), 7.11-7.04 (m, 3H), 6.89 (dd, *J* = 6.8, 2.0 Hz, 2H), 4.41-4.35 (m, 1H), 3.82 (s, 3H), 3.55 (s, 2H), 3.07 (d, *J* = 10.0 Hz, 2H), 2.50 (d, *J* = 8.8 Hz, 2H), 2.18 (t, *J* = 10.0 Hz, 2H), 1.81 (dd, *J* = 12.2, 1.8 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{24}N_3O_2$ is 338.18, found 338.03; HPLC t_R = 3.26 min.

***N*-(4-((4-(2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)-piperidin-1-yl)methyl)phenyl)acetamide**, (**8**)



This compound was prepared according to the procedure for compound **2** in 34% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (s, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.33-7.28 (m, 3H), 7.10-7.04 (m, 3H), 4.36 (tt, *J* = 12.6, 4.0 Hz, 1H), 3.54 (s, 2H), 3.03 (d, *J* = 11.6 Hz, 2H), 2.48 (q, *J* = 12.4 Hz, 2H), 2.16-2.12 (m, 5H), 1.79 (d, *J* = 10.4 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{21}H_{25}N_4O_2$ is 365.19, found 365.06; HPLC t_R = 3.09 min.

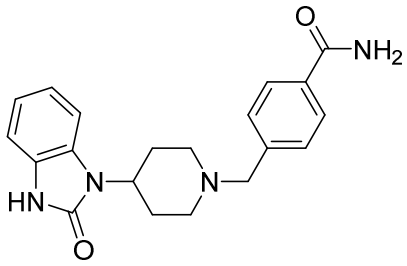
(4-((4-(2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)-piperidin-1-yl)methyl)benzonitrile, (**9**)



A mixture of 1-(piperidin-4-yl)-1H-benzo[d]imidazol-2(3H)-one (40 mg, 0.1 mmol), 4-cyanobenzyl bromide (24 mg, 0.1 mmol), K_2CO_3 (20 mg, 0.1 mmol), and acetonitrile (1.2 mL) was stirred at 80 ^{o}C for 24 h. Upon completion, the solvent was removed under reduced pressure. Purification via silica gel chromatography afforded pure product **9** (30 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.28-7.27 (m, 1H), 7.11-7.05 (m, 3H), 4.40-4.34 (m, 1H), 3.62 (s, 2H), 3.00 (d, *J*

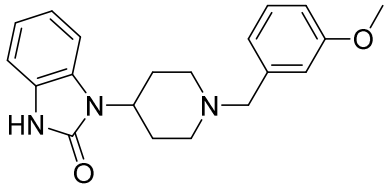
= 9.6 Hz, 2H), 2.50 (q, *J* = 11.6 Hz, 2H), 2.23 (t, *J* = 11.2 Hz, 2H), 1.83 (d, *J* = 10.0 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{21}N_4O$ is 333.16, found 333.05; HPLC t_R = 3.29 min.

(4-((4-(2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)-piperidin-1-yl)methyl)benzamide, (**10**)



Hydrogen peroxide (50%, 28 μL, 0.5 mmol) was added to a solution of compound **9** (16 mg, 0.05 mmol) and NaOH (3M, 17 μL, 0.05 mmol) in EtOH (2.5 mL). The reaction mixture was stirred overnight at room temperature and then concentrated to dryness. Purification via silica gel chromatography afforded pure product **10** (5.0 mg, 30% yield). ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.96 (s, 1H), 8.05 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.47 (s, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 6.96 (td, *J* = 7.6, 1.6 Hz, 2H), 6.91 (qd, *J* = 7.4, 1.6 Hz, 1H), 4.70 (s, 2H), 4.47 (tt, *J* = 12.4, 4.4 Hz, 1H), 3.68 (t, *J* = 11.6 Hz, 2H), 3.36 (d, *J* = 10.0 Hz, 2H), 2.97 (dd, *J* = 12.6, 9.6 Hz, 2H), 1.75 (d, *J* = 13.2 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{23}N_4O_2$ is 351.17, found 351.07; HPLC t_R = 2.93 min.

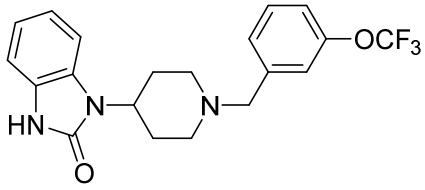
1-(1-(3-Methoxybenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**11**)[4]



This compound was prepared according to the procedure for compound **2** in 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.04 (s, 1H), 7.31-7.24 (m, 2H), 7.13-7.11 (m, 1H), 7.05 (t, *J* = 4.0 Hz, 2H), 6.96 (d, *J* = 6.8 Hz, 2H), 6.82 (dd, *J* = 7.6, 1.6 Hz, 1H),

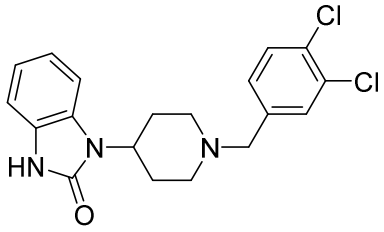
4.39 (tt, *J* = 12.4, 4.0 Hz, 1H), 3.84 (s, 3H), 3.58 (s, 2H), 3.08 (d, *J* = 10.8 Hz, 2H), 2.52 (q, *J* = 12.0 Hz, 2H), 2.21 (t, *J* = 11.2 Hz, 2H), 1.81 (d, *J* = 10.4 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{24}N_3O_2$ is 338.18, found 338.08; HPLC t_R = 3.38 min.

1-(1-(3-(Trifluoromethoxy)benzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**12**)



This compound was prepared according to the procedure for compound **2** in 43% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 (s, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.32-7.28 (m, 3H), 7.16-7.12 (m, 2H), 7.08-7.06 (m, 2H), 4.40 (tt, *J* = 12.4, 4.0 Hz, 1H), 3.60 (s, 2H), 3.04 (d, *J* = 11.6 Hz, 2H), 2.51 (qd, *J* =12.6, 3.8 Hz, 2H), 2.22 (td, *J* =11.8, 2.0 Hz, 2H), 1.83 (dd, *J* = 12.0, 2.0 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{21}F_3N_3O_2$ is 392.15, found 392.06; HPLC t_R = 3.99 min.

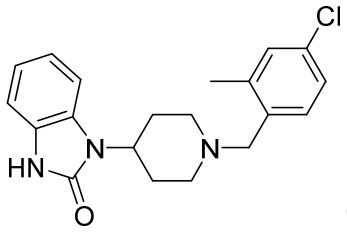
1-(1-(3,4-Dichlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**13**)



This compound was prepared according to the procedure for compound **2** in 13% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 7.49 (d *J* = 1.6 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.28 (dd, *J* = 6.0, 2.8 Hz, 1H), 7.22 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.14-7.11 (m, 1H), 7.08-7.07 (m, 2H), 4.38 (tt, *J* = 12.4, 4.0 Hz, 1H), 3.51 (s, 2H), 3.01 (d, *J* = 11.6 Hz,

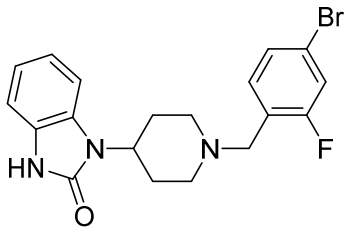
2H), 2.49 (qd, *J* = 12.4, 4.0 Hz, 2H), 2.20 (td, *J* = 11.8, 2.0 Hz, 2H), 1.82 (dd, *J* = 12.0, 2.4 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{20}Cl_2N_3O$ is 376.09, found 376.11; HPLC t_R = 3.98 min.

1-(1-(4-Chloro-2-Methylbenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**14**)



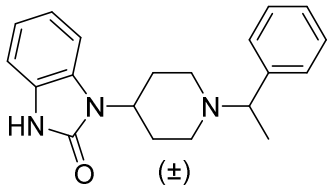
This compound was prepared according to the procedure for compound **2** in 23% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (s, 1H), 7.23 (d, *J* = 6.0 Hz, 2H), 7.17-7.05 (m, 5H), 4.38 (tt, *J* = 12.6, 4.0 Hz, 1H), 3.47 (s, 2H), 3.01 (d, *J* = 11.2 Hz, 2H), 2.44 (qd, *J* = 12.4, 3.8 Hz, 2H), 2.40 (s, 3H), 2.20 (t, *J* = 11.2 Hz, 2H), 1.80 (dd, *J* = 11.0, 2.0 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{23}ClN_3O$ is 356.15, found 356.14; HPLC t_R = 3.73 min.

1-(1-(4-Bromo-2-fluorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**15**)



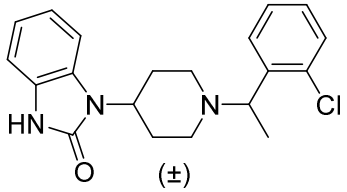
This compound was prepared according to the procedure for compound **2** in 33% yield. ^{1}H NMR (400 MHz, CD_3OD) δ 7.40-7.35 (m, 4H), 7.06-7.04 (m, 3H), 4.30 (tt, *J* = 12.4, 4.4 Hz, 1H), 3.65 (d, *J* = 1.2 Hz, 2H), 3.09 (dd, *J* = 9.8, 1.8 Hz, 2H), 2.53 (qd, *J* = 12.8, 4.0 Hz, 2H), 2.29 (td, *J* = 12.2, 2.0 Hz, 2H), 1.76 (dd, *J* = 12.0, 2.4 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{19}BrFN_3O$ is 404.07, found 404.23; HPLC t_R = 3.74 min.

1-(1-(1-(Phenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**16**)[5]



This compound was prepared according to the procedure for compound **1** in 74% yield. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.80 (s, 1H), 7.34 (t, *J* = 3.0 Hz, 4H), 7.26-7.19 (m, 2H), 6.99-6.95 (m, 3H), 4.05 (tt, *J* = 12.6, 4.0 Hz, 1H), 3.53 (q, *J* = 6.8 Hz, 1H), 3.10 (d, *J* = 10.0 Hz, 1H), 2.89 (d, *J* = 9.6 Hz, 1H), 2.45-2.23 (m, 2H), 2.07 (td, *J* = 10.4, 2.4 Hz, 1H), 1.97 (td, *J* = 10.8, 2.0 Hz, 1H), 1.66 (d, *J* = 10.8 Hz, 1H), 1.58 (d, *J* = 10.4 Hz, 1H), 1.33 (d, *J* = 6.8 Hz, 3H); MS(*m/z*): [M + H] calc'd for $C_{20}H_{24}N_3O$ is 322.18, found 321.96; HPLC t_R = 3.52 min.

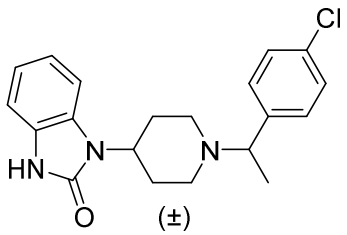
1-(1-(1-(2-Chlorophenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**17**)[6]



A mixture of 1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one (20 mg, 0.06 mmol), 2′-chloroacetophenone (36 mg, 0.2 mmol), and Ti(O*i*Pr)$_4$ (0.2 mL, 0.6 mmol) was stirred at 50 ^{o}C for 24 h under argon and then was cooled to room temperature. A mixture of $NaCNBH_3$ (11 mg, 0.2 mmol) in EtOH (0.2 mL) was then added dropwise and the reaction mixture was stirred overnight at room temperature. Upon completion, the solvent was removed under reduced pressure. Purification via silica gel chromatography afforded pure product **17** (13 mg, 61% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.66 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.41 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.38-7.33 (m, 2H), 7.26 (td, *J* = 7.6, 1.6 Hz, 1H), 7.09-7.04 (m,

3H), 4.29 (tt, *J* = 12.4, 4.0 Hz, 1H), 4.20 (q, *J* = 6.8 Hz, 1H), 3.49 (dt *J* = 12.0, 1.8 Hz, 1H), 3.02 (dd, *J* = 11.6, 2.8 Hz, 1H), 2.62 (qd, *J* = 12.6, 4.0 Hz, 1H), 2.46 (qd, *J* = 12.4, 4.0 Hz, 1H), 2.37 (td, *J* = 12.2, 2.4 Hz, 1H), 2.26 (td, *J* = 12.2, 2.4 Hz, 1H), 1.84 (dq, *J* = 12.8, 2.4 Hz, 1H), 1.69 (dq, *J* = 12.8, 2.4 Hz, 1H), 1.43 (d, *J* = 6.8 Hz, 3H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{23}ClN_3O$ is 356.15, found 356.10; HPLC t_R = 3.57 min.

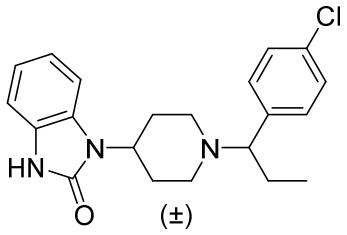
1-(1-(1-(4-Chlorophenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**18**)[7]



$Ti(OiPr)_4$ (0.3 mL, 1.0 mmol) was added to a solution of 1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one (free base, 0.1 g, 0.5 mmol) and 4′-chloroacetophenone (78 µL, 0.6 mmol) in THF (5 mL). The reaction mixture was stirred at 80 °C for 5 h under argon and then was cooled to room temperature. $NaBH(OAc)_3$ (0.3 g, 1.5 mmol) was then added and the reaction mixture was stirred overnight at room temperature. The reaction mixture was quenched with saturated $NaHCO_3$ and then was filtered through a pad of Celite®. The filtrate was concentrated to dryness and the aqueous layer was extracted with CH_2Cl_2; the combined organic layers were dried over Na_2SO_4 and concentrated to dryness. Purification via silica gel chromatography afforded pure product **18** (31 mg, 19% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.19 (td, *J* = 7.6, 1.2 Hz, 1H), 7.09-7.02 (m, 2H), 4.62-4.54 (m, 1H), 4.21-4.18 (m, 1H), 3.89 (d, *J* = 10.4 Hz, 1H), 3.52 (d, *J* = 12.8 Hz, 2H), 3.27 (qd, *J* = 11.6, 4.0 Hz, 1H), 2.78 (q, *J* = 10.4 Hz, 1H),

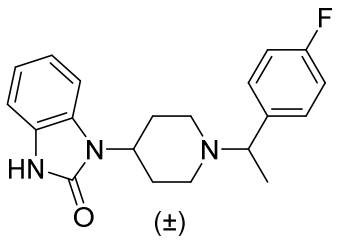
2.65 (q, J = 11.2 Hz, 1H), 1.97 (d, J = 6.8 Hz, 3H), 1.93-1.89 (m, 2H); MS(*m/z*): [M + H] calc'd for $C_{20}H_{23}ClN_3O$ is 356.15, found 355.92; HPLC t_R = 3.76 min.

1-(1-(1-(4-Chlorophenyl)propyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**19**)[7]



This compound was prepared according to the procedure for compound **18** in 10% yield. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.79 (s, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.18 (dd, J = 4.2, 2.0 Hz, 1H), 6.99-6.94 (m, 3H), 4.57-4.45 (m, 1H), 3.97 (t, J = 12.2 Hz, 1H), 3.07 (dd, J = 10.8, 3.6 Hz, 1H), 2.92 (d, J = 9.2 Hz, 1H), 2.39-2.24 (m, 2H), 2.18 (t, J = 7.2 Hz, 1H), 2.02 (t, J = 11.6 Hz, 1H), 1.90-1.68 (m, 2H), 1.64-1.57 (m, 2H), 0.74 (t, J = 7.2 Hz, 3H); MS(*m/z*): [M+H] calc'd for $C_{21}H_{25}ClN_3O$ is 370.16, found 370.10; HPLC t_R = 3.95 min.

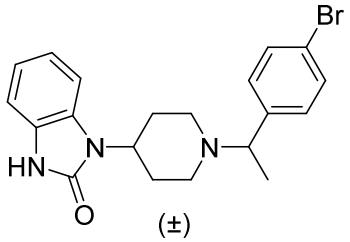
1-(1-(1-(4-Fluorophenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**20**)[7]



This compound was prepared according to the procedure for compound **18** in 51% yield. ^{1} H NMR (400 MHz, $CDCl_3$) δ 10.26 (s, 1H), 7.33 (dd, J = 8.4, 2.8 Hz, 2H), 7.29-7.28 (m, 1H), 7.13-7.01 (m, 5H), 4.31 (tt, J = 12.6, 4.0 Hz, 1H), 3.52 (q, J = 5.8

Hz, 1H), 3.20 (d, *J* = 10.4 Hz, 1H), 2.96 (d, *J* = 10.4 Hz, 1H), 2.54-2.37 (m, 2H), 2.18 (t, *J* = 11.2 Hz, 1H), 2.07 (t, *J* = 12.0 Hz, 1H), 1.84 (dd, *J* = 12.4, 1.6 Hz, 1H), 1.75 (dd, *J* = 12.4, 1.6 Hz, 1H), 1.40 (d, *J* = 6.4 Hz, 3H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{23}FN_3O$ is 340.17, found 339.96; HPLC t_R = 3.41 min.

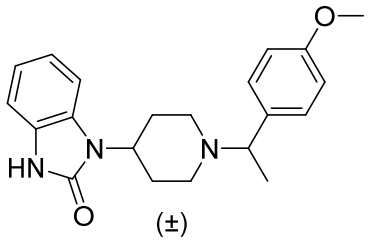
1-(1-(1-(4-Bromophenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**21**)



(±)

This compound was prepared according to the procedure for compound **17** in 88% yield. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.84 (s, 1H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.20 (dd, *J* = 5.6, 2.4 Hz, 1H), 6.98-6.95 (m, 3H), 4.05 (tt, *J* = 12.2, 4.0 Hz, 1H), 3.54 (q, *J* = 6.8 Hz, 1H), 3.06 (d, *J* = 10.8 Hz, 1H), 2.86 (d, *J* = 10.0 Hz, 1H), 2.33 (qd, *J* = 12.2, 4.0 Hz, 2H), 2.06 (t, *J* = 10.8 Hz, 1H), 1.97 (t, *J* = 11.0 Hz, 1H), /1.65 (d, *J* = 10.4 Hz, 1H), 1.58 (d, *J* = 11.2 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 3H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{23}BrN_3O$ is 400.09, found 400.10; HPLC t_R = 3.93 min.

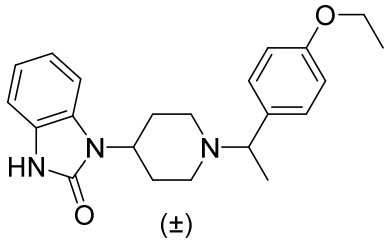
1-(1-(1-(4-Methoxyphenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**22**)



(±)

This compound was prepared according to the procedure for compound **18** in 40% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.20-7.18 (m, 2H), 7.00-6.96 (m, 4H), 6.80 (d, *J* = 7.2 Hz, 2H), 4.22-4.16 (m, 1H), 3.74 (s, 3H), 3.41 (q, *J* = 5.2 Hz, 1H), 3.10 (d, *J* = 10.0 Hz, 1H), 2.89 (d, *J* = 10.4 Hz, 1H), 2.40-2.28 (m, 2H), 2.08 (t, *J* = 12.2 Hz, 1H), 1.96 (t, *J* = 12.6 Hz, 1H), 1.77-1.65 (m, 2H), 1.31 (d, *J* = 5.6 Hz, 3H); MS(*m/z*): [M+H] calc'd for $C_{21}H_{26}N_3O_2$ is 352.19, found 351.98; HPLC t_R = 3.56 min.

1-(1-(1-(4-Ethoxyphenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**23**)

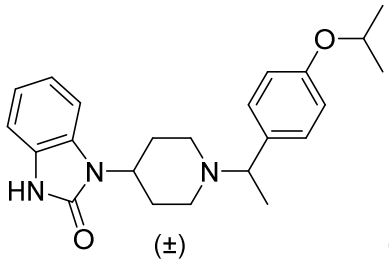


(±)

This compound was prepared according to the procedure for compound **18** in 58% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.89 (s, 1H), 7.29 (d, *J* = 8.8 Hz, 3H), 7.17-7.14 (m, 1H), 7.07-7.05 (m, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 4.34 (tt, *J* = 12.6, 4.0 Hz, 1H), 4.07 (q, *J* = 6.8 Hz, 2H), 3.55 (q, *J* = 6.6 Hz, 1H), 3.24 (d, *J* = 10.8 Hz, 1H), 3.04 (d, *J* = 10.8 Hz, 1H), 2.55 (qd, *J* = 12.0, 3.2 Hz, 1H), 2.45 (qd, *J* = 12.0, 3.2 Hz, 1H), 2.21 (t, *J* = 11.0 Hz, 1H), 2.10 (t, *J* = 11.0 Hz, 1H), 1.86 (dd, *J* = 12.4, 1.6 Hz, 1H), 1.78 (dd, *J* = 12.6, 1.8 Hz,

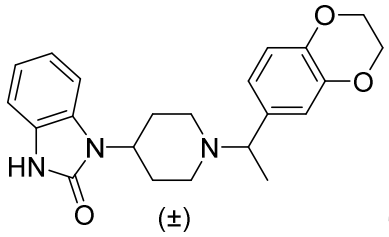
1H), 1.47-1.44 (m, 6H); MS(*m/z*): [M+H] calc'd for $C_{22}H_{28}N_3O_2$ is 366.21, found 365.96; HPLC t_R = 3.64 min.

1-(1-(1-(4-(*Iso*propoxy)phenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**24**)



This compound was prepared according to the procedure for compound **17** in 65% yield. ^{1}H NMR (400 MHz, CD_3OD) δ 7.38 (d, *J* = 8.8 Hz, 2H), 7.32-7.29 (m, 1H), 7.09-7.06 (m, 3H), 6.98 (d, *J* = 8.8 Hz, 2H), 4.63 (septet, *J* = 6.0 Hz, 1H), 4.40-4.37 (m, 1H), 4.16 (q, *J* = 7.2 Hz, 1H), 3.61 (d, *J* = 8.4 Hz, 1H), 3.35 (dd, *J* = 10.4, 3.2 Hz, 1H), 2.82-2.60 (m, 4H), 2.01-1.90 (m, 2H), 1.67 (d, *J* = 6.8 Hz, 3H), 1.32 (d, *J* = 6.0 Hz, 6H); MS(*m/z*): [M+H] calc'd for $C_{23}H_{30}N_3O_2$ is 380.23, found 379.94; HPLC t_R = 3.86 min.

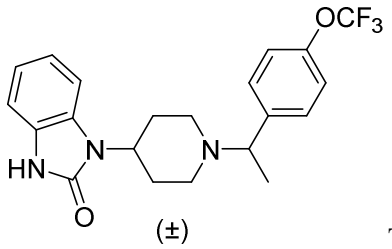
1-(1-(1-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**25**)[2]



This compound was prepared according to the procedure for compound **18** in 56% yield. Methane sulfonic acid (17 μL, 0.3 mmol) was added to a suspension of **25** in EtOH (1 mL). The mixture was heated to 60 ^{o}C for 30 min. The solvent was removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was

frozen and then subjected to lyophilization overnight giving product **25** in the form of a mesylate salt. ^{1}H NMR mesylate (400 MHz, CD_3OD) δ 7.29-7.26 (m, 1H), 7.10-7.06 (m, 4H), 7.01 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 4.51-4.41 (m, 2H), 4.28 (s, 4H), 3.84 (dd, *J* = 11.6, 2.2 Hz, 1H), 3.49 (dd, *J* = 11.6, 2.8 Hz, 1H), 3.14 (td, *J* = 13.0, 2.8 Hz, 1H), 3.04 (td, *J* = 13.0, 2.8 Hz, 1H), 2.88-2.77 (m, 2H), 2.72 (s, 3H), 2.12-2.01 (m, 2H), 1.77 (d, *J* = 6.8 Hz, 3H); MS(*m/z*): [M + H] calc'd for $C_{22}H_{26}N_3O_3$ is 380.19, found 379.87; HPLC t_R = 4.58 min.

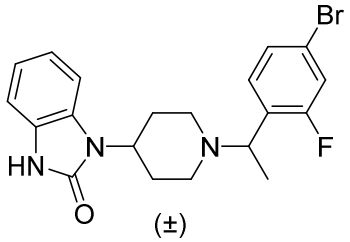
1-(1-(1-(4-(Trifluoromethoxy)phenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**26**)



(±)

This compound was prepared according to the procedure for comopound **18** in 8% yield. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.82 (s, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 6.4 Hz, 1H), 7.00-6.96 (m, 3H), 4.07 (tt, *J* = 12.0, 4.0 Hz, 1H), 3.60 (q, *J* = 6.6 Hz, 1H), 3.07 (d, *J* = 10.4, 1H), 2.86 (d, *J* = 10.8 Hz, 1H), 2.33 (sextet d, *J* = 12.4, 3.8 Hz, 2H), 2.08 (t, *J* = 11.8 Hz, 1H), 2.00 (t, *J* = 10.8 Hz, 1H), 1.66 (d, *J* = 12.4 Hz, 1H), 1.59 (d, *J* = 10.8 Hz, 1H), 1.32 (d, *J* = 6.8 Hz, 3H); MS(*m/z*): [M + H] calc'd for $C_{21}H_{23}F_3N_3O_2$ is 406.17; found 405.96; HPLC t_R = 3.96 min.

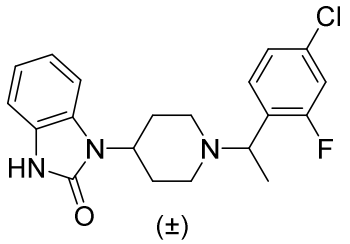
1-(1-(1-(4-Bromo-2-fluorophenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**27**)



(±)

This compound was prepared according to the procedure for compound **18** in 7% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.30-7.22 (m, 3H), 7.08-7.06 (m, 3H), 4.30-4.23 (m, 1H), 3.91 (q, *J* = 6.4 Hz, 1H), 3.25 (d, *J* = 10.8 Hz, 1H), 2.97 (d, *J* = 10.8 Hz, 1H), 2.50 (qd, *J* = 12.2, 3.6 Hz, 1H), 2.37 (qd, *J* = 12.4, 3.2 Hz, 1H), 2.17 (t, *J* = 11.4 Hz, 1H), 2.02 (t, *J* = 11.6 Hz, 1H), 1.84 (d, *J* = 11.2 Hz, 1H), 1.74 (d, *J* = 12.0 Hz, 1H), 1.39 (d, *J* = 6.4 Hz, 3H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{22}BrFN_3O$ is 418.09, found 418.16; HPLC t_R = 3.94 min.

1-(1-(1-(4-Chloro-2-fluorophenyl)ethyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**28**)

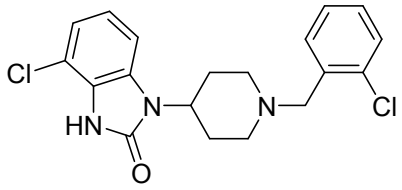


(±)

This compound was prepared according to the procedure for compound **18** in 33% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15 (s, 1H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.28-7.27 (m, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.13-7.04 (m, 4H), 4.32-4.26 (m, 1H), 3.94 (q, *J* = 6.8 Hz, 1H), 3.26 (d, *J* = 8.8 Hz, 1H), 2.99 (d, *J* = 8.8 Hz, 1H), 2.51 (d, *J* = 10.8 Hz, 1H), 2.40 (d, *J* = 10.8 Hz, 1H), 2.19 (t, *J* = 9.6 Hz, 1H), 2.03 (t, *J* = 10.6 Hz, 1H), 1.87 (t, *J* = 13.8

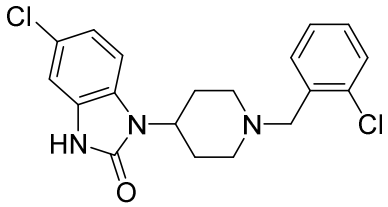
Hz, 1H), 1.76 (d, J = 11.6 Hz, 1H), 1.41 (d, J = 5.6 Hz, 3H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{22}ClFN_3O$ is 374.14, found 374.09; HPLC t_R = 3.71 min.

4-Chloro-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**29**)[8]



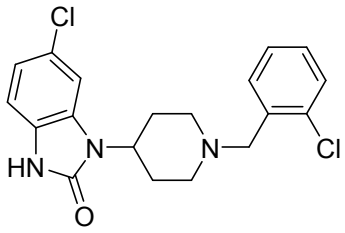
CDI (49 mg, 0.3 mmol) was slowly added to a solution of **VIII** (70 mg, 0.2 mmol) in THF (4 mL). The reaction mixture was stirred overnight at room temperature under argon and then quenched with 10% HCl $_{(aq)}$. The aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na_2SO_4 and concentrated to dryness. Purification via silica gel chromatography afforded pure product **29** (61 mg, 81% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.71 (dd, J = 7.4, 1.8 Hz, 1H), 7.62 (dd, J = 8.0, 1.6 Hz, 1H), 7.57-7.47 (m, 2H), 7.22 (dd, J = 7.0, 1.8 Hz, 1H), 7.11-7.03 (m, 2H), 4.65-4.55 (m, 3H), 3.73 (d, J = 12.0 Hz, 2H), 3.43 (t, J = 12.2 Hz, 2H), 2.81 (d, J = 13.2 Hz, 2H), 2.09 (d, J =14.8 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{20}Cl_2N_3O$ is 376.09, found 376.20; HPLC t_R = 3.49 min.

5-Chloro-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**30**)



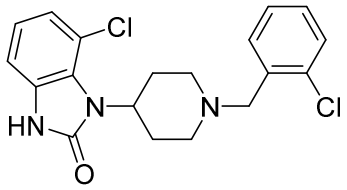
This compound was prepared according to the procedure for compound **2** in 39% yield from 5-chloro-1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 11.03 (s, 1H), 7.57 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.44 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.36 (td, *J* = 7.4, 1.4 Hz, 1H), 7.29 (td, *J* = 7.5, 2.0 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.01 (td, *J* = 9.6, 2.0 Hz, 2H), 4.16 (tt, *J* = 12.0, 4.4 Hz, 1H), 3.62 (s, 2H), 2.96 (d, *J* = 11.2 Hz, 2H), 2.34 (qd, *J* = 12.4, 3.4 Hz, 2H), 2.21 (t, *J* = 11.0 Hz, 2H), 1.65 (dd, *J* = 11.6, 2.0 Hz, 2H); MS(*m/z*): [M + H] calc'd for $C_{19}H_{20}Cl_2N_3O$ is 376.09, found 376.00; HPLC t_R = 3.87 min.

6-Chloro-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**31**)



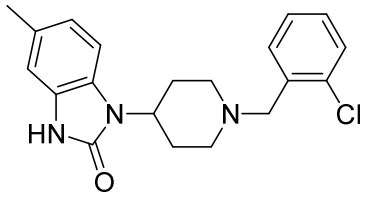
This compound was prepared according to the procedure for compound **29** in 56% yield from 5-chloro-N^1-(1-(2-chlorobenzyl)piperidin-4-yl)benzene-1,2-diamine. ^{1}H NMR (400 MHz, CD_3OD) δ 7.70 (dd, *J* = 7.4, 2.2 Hz, 1H), 7.63 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.55 (td, *J* = 7.4, 2.0 Hz, 1H), 7.50 (td, *J* = 7.4, 1.6 Hz, 1H), 7.37 (d, *J* = 1.6 Hz, 1H), 7.08 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 4.61-4.55 (m, 3H), 3.74 (d, *J*= 12.4 Hz, 2H), 3.43 (t, *J* = 12.2 Hz, 2H), 2.78 (q, *J* = 12.0 Hz, 2H), 2.09 (d, *J* = 12.8 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{20}Cl_2N_3O$ is 376.09, found 376.13; HPLC t_R = 3.81 min.

7-Chloro-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**32**)



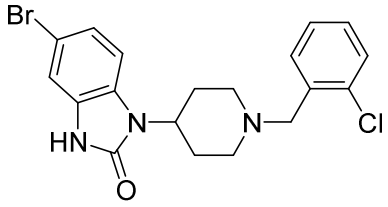
This compound was prepared according to the procedure for compound **29** in 9% yield from 6-chloro-N^1-(1-(2-chlorobenzyl)piperidin-4-yl)benzene-1,2-diamine. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.46 (t, *J* = 4.6 Hz, 1H), 7.40-7.38 (m, 2H), 7.06-7.00 (m, 4H), 5.23-5.16 (m, 1H), 4.55 (s, 2H), 3.81 (d, *J* = 8.0 Hz, 2H), 3.30 (t, *J* = 11.4 Hz, 2H), 2.94 (t, *J* = 10.8 Hz, 2H), 2.06 (d, *J*= 10.0 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{20}Cl_2N_3O$ is 376.09, found 376.13; HPLC t_R = 3.91 min.

5-Methyl-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**33**)[8]



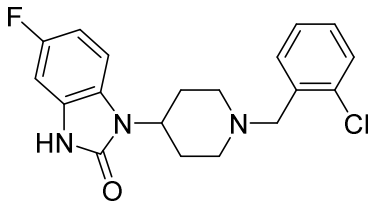
This compound was prepared according to the procedure for compound **29** in 56% yield from 4-methyl-N^1-(1-(2-chlorobenzyl)piperidin-4-yl)benzene-1,2-diamine. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.54 (d, *J* = 5.6 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.20-7.15 (m, 2H), 6.89-6.86 (m, 2H), 4.37-4.31 (m, 1H), 3.68 (s, 2H), 3.07 (d, *J* = 10.8 Hz, 2H), 2.45 (t, *J* = 12.0 Hz, 2H), 2.37 (s, 3H), 2.29 (t, *J* = 10.8 Hz, 2H), 1.80 (d, *J* = 13.2 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{23}ClN_3O$ is 356.15, found 356.13; HPLC t_R = 3.74 min.

5-Bromo-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**34**)



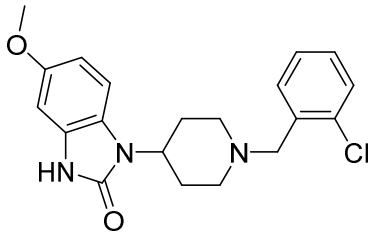
This compound was prepared according to the procedure for compound **2** in 29% yield from 5-bromo-1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. ^{1}H NMR (400 MHz, CD_3OD) δ 7.56 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.42 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.39-7.37 (m, 1H), 7.33 (td, *J* = 7.4, 1.8 Hz, 1H), 7.28 (td, *J* = 7.4, 1.8 Hz, 1H), 7.07-7.04 (m, 2H), 4.33 (tt, *J* = 12.2, 4.6 Hz, 1H), 3.75 (s, 2H), 3.14 (dd, *J* = 9.6, 2.0 Hz, 2H), 2.55 (qd, *J* = 12.6, 3.8 Hz, 2H), 2.36 (td, *J* =12.2, 2.0 Hz, 2H), 1.76 (dd, *J* = 12.2, 2.6 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{20}BrClN_3O$ is 420.04, found 420.02; HPLC t_R = 3.91 min.

5-Fluoro-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**35**)



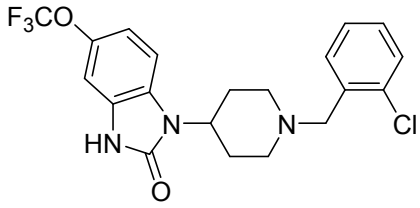
This compound was prepared according to the procedure for compound **2** in 22% yield from 5-fluoro-1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. ^{1}H NMR (400 MHz, CD_3OD) δ 7.55 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.41 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.35-7.25 (m, 3H), 6.84-6.78 (m, 2H), 4.30 (tt, *J* = 12.4, 4.4 Hz, 1H), 3.73 (s, 2H), 3.12 (dd, *J* = 9.6, 2.0 Hz, 2H), 2.50 (qd, *J* = 12.6, 3.6 Hz, 2H), 2.33 (td, *J* = 12.0, 2.0 Hz, 2H), 1.75 (dd, *J* = 12.2, 2.2 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{20}ClFN_3O$ is 360.12, found 360.10; HPLC t_R = 3.88 min.

5-Methoxy-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**36**)



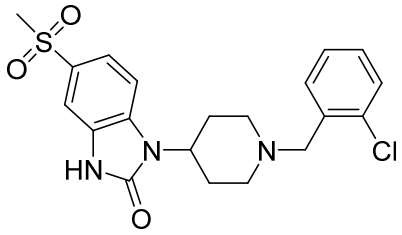
This compound was prepared according to the procedure for compound **29** in 11% yield from 4-methoxy-N^1-(1-(2-chlorobenzyl)piperidin-4-yl)benzene-1,2-diamine. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 7.80 (dd, J = 5.4, 1.6 Hz, 1H), 7.49-7.46 (m, 1H), 7.43-7.37 (m, 3H), 6.65 (d, J = 8.4 Hz, 2H), 4.68-4.63 (m, 1H), 4.48 (s, 2H), 3.78 (s, 3H), 3.73 (d, J = 10.4 Hz, 2H), 3.01 (t, J = 12.0 Hz, 2H), 2.94 (t, J = 12.8 Hz, 2H), 1.98 (d, J = 12.0 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{23}ClN_3O_2$ is 372.14, found 372.11; HPLC t_R = 3.60 min.

5-(Trifluoromethoxy)-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**37**)



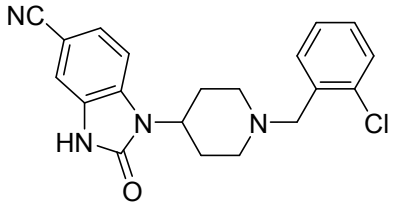
This compound was prepared according to the procedure for compound **29** in 83% yield from 4-(trifluoromethoxy)-N^1-(1-(2-chlorobenzyl)piperidin-4-yl)benzene-1,2-diamine. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 7.78 (t, J = 4.8 Hz, 1H), 7.52-7.40 (m, 4H), 6.98 (s, 1H), 4.73-4.68 (m, 1H), 4.50 (s, 2H), 3.75 (d, J = 11.2 Hz, 2H), 3.03 (t, J = 12.4 Hz, 2H), 2.91 (q, J = 12.0 Hz, 2H), 2.00 (d, J = 11.6 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{20}ClF_3N_3O_2$ is 426.11, found 426.13; HPLC t_R = 4.00 min.

5-(Methylsulfonyl)-1-(1-(2-chlorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**38**)



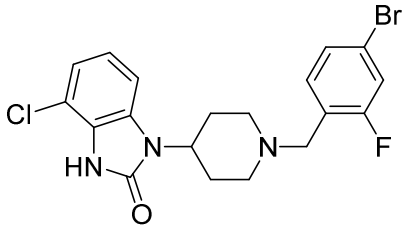
This compound was prepared according to the procedure for compound **29** in 75% yield from 4-(methylsulfonyl)-N^1-(1-(2-chlorobenzyl)piperidin-4-yl)benzene-1,2-diamine. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.03 (t, *J* = 8.8 Hz, 2H), 7.77 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.70 (d, *J* = 1.6 Hz, 1H), 7.51-7.43 (m, 3H), 4.82-4.75 (m, 1H), 4.48 (s, 2H), 3.73 (d, *J* = 11.6 Hz, 2H), 3.19 (t, *J* = 13.6 Hz, 2H), 3.09 (q, *J* = 11.4 Hz, 2H), 3.04 (s, 3H), 2.03 (d, *J* = 12.0 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{23}ClN_3O_3S$ is 420.11, found 420.12; HPLC t_R = 3.28 min.

1-(1-(2-Chlorobenzyl)piperidin-4-yl)-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazole-5-carbonitrile, (**39**)



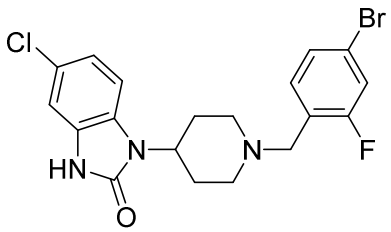
This compound was prepared according to the procedure for compound **29** in 70% yield from 3-amino-4-((1-(2-chlorobenzyl)piperidin-4-yl)amino)benzonitrile. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.52 (d, *J* = 3.6 Hz, 1H), 7.42-7.36 (m, 4H), 7.30-7.22 (m, 2H), 4.41-4.35 (m, 1H), 4.38 (s, 2H), 3.10 (d, *J* = 7.2 Hz, 2H), 2.44 (t, *J* = 10.0 Hz, 2H), 2.32 (t, *J* = 10.8 Hz, 2H), 1.83 (d, *J* = 10.8 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{20}ClN_4O$ is 367.12, found 367.14; HPLC t_R = 3.50 min.

4-Chloro-1-(1-(4-bromo-2-fluorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**40**)[8]



This compound was prepared according to the procedure for compound **17** in 35% yield from 4-chloro-1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. Methane sulfonic acid (4.0 μL, 0.06 mmol) was added to a suspension of **40** in EtOH (1 mL). The mixture was heated to 60 ^{o}C for 30 min. The solvent was removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was frozen and then subjected to lyophilization overnight giving product **40** in the form of a mesylate salt. ^{1}H NMR mesylate (400 MHz, CD_3OD) δ 7.61 (dd, *J* = 9.2, 1.2 Hz, 1H), 7.57 (dd, *J* = 3.8, 1.4 Hz, 2H), 7.20 (dd, *J* = 6.0, 2.8 Hz, 1H), 7.09-7.07 (m, 2H), 4.54 (tt, *J* = 12.2, 4.2 Hz, 1H), 4.45 (s, 2H), 3.71 (d, *J* = 12.8 Hz, 2H), 3.36-3.30 (m, 2H), 2.80 (qd, *J* = 3.4 Hz, 2H), 2.71 (s, 3H), 2.10 (d, *J* = 12.4 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{19}BrClFN_3O$ is 438.03, found 437.99; HPLC t_R = 4.01 min.

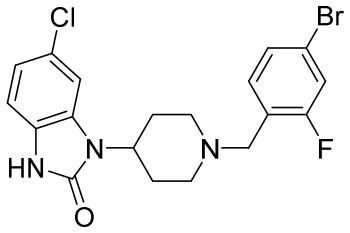
5-Chloro-1-(1-(4-bromo-2-fluorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**41**)[8]



This compound was prepared according to the procedure for compound **2** in 63% yield from 5-chloro-1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. Methane sulfonic acid (65 μL, 1.0 mmol) was added to a suspension of **41** in EtOH (1 mL). The

mixture was heated to 60 ^{o}C for 30 min. The solvent was removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was frozen and then subjected to lyophilization overnight giving product **41** in the form of a mesylate salt. ^{1}H NMR mesylate (400 MHz, CD_3OD) δ 7.61 (dd, *J* = 8.8, 0.8 Hz, 1H), 7.57 (dd, *J* = 3.8, 1.4 Hz, 2H), 7.23 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.10 (d, *J* = 2.0 Hz, 1H), 7.08 (d, *J* = 1.2 Hz, 1H), 4.53 (tt, *J* = 12.4, 4.0 Hz, 1H), 4.45 (s, 2H), 3.70 (d, *J* = 12.8 Hz, 2H), 3.36-3.29 (m, 2H), 2.79 (qd, *J* = 13.0, 3.4 Hz, 2H), 2.72 (s, 3H), 2.09 (d, *J* = 14.0 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{19}BrClFN_3O$ is 438.03, found 438.11; HPLC t_R = 3.66 min.

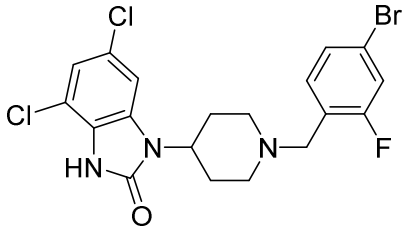
6-Chloro-1-(1-(4-bromo-2-fluorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**42**)[8]



This compound was prepared according to the procedure for compound **17** in 32% yield from 6-chloro-1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. Methane sulfonic acid (6.0 μL, 0.1 mmol) was added to a suspension of **42** in EtOH (1 mL). The mixture was heated to 60 ^{o}C for 30 min. The solvent was removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was frozen and then subjected to lyophilization overnight giving product **42** in the form of a mesylate salt. ^{1}H NMR mesylate (400 MHz, CD_3OD) δ 7.61 (dd, *J* = 10.0, 1.2 Hz, 1H), 7.57 (dd, *J* = 3.6, 1.2 Hz, 2H), 7.36 (d, *J* = 2.0 Hz, 1H), 7.08 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 4.55 (tt, *J* = 12.4, 4.0 Hz, 1H), 4.45 (s, 2H), 3.71 (d, *J* = 12.4 Hz, 2H), 3.36-3.32 (m, 2H), 2.77 (qd, *J* = 13.0,

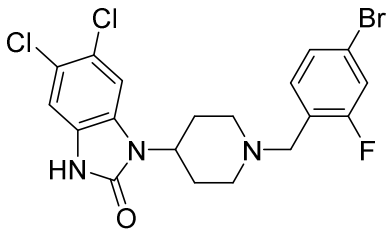
3.6 Hz, 2H), 2.72 (s, 3H), 2.10 (d, J = 14.8 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{19}BrClFN_3O$ is 438.03, found 437.96; HPLC t_R = 4.08 min.

4,6-Dichloro-1-(1-(4-bromo-2-fluorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**43**)



This compound was prepared according to the procedure for compound **17** in 68% yield from 4,6-dichloro-1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. A solution of methane sulfonic acid in EtOH (0.06 M, 1.0 mL, 0.06 mmol) was added to **43**. The solvent was removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was frozen and then subjected to lyophilization overnight giving product **43** in the form of a mesylate salt. ^{1}H NMR mesylate (400 MHz, CD_3OD) δ 7.59-7.54 (m, 3H), 7.34 (d, J = 1.6 Hz, 1H), 7.13 (d, J = 5.0 Hz, 1H), 4.50 (tt, J = 12.4, 4.0 Hz, 1H), 4.36 (s, 2H), 3.62 (d, J = 12.4 Hz, 2H), 3.20 (t, J = 12.4 Hz, 2H), 2.79-2.72 (m, 5H), 2.05 (d, J = 12.4 Hz, 2H); MS(*m/z*): [M + H] calc'd for $C_{19}H_{18}BrCl_2FN_3O$ is 471.99, found 472.10; HPLC t_R = 3.76 min.

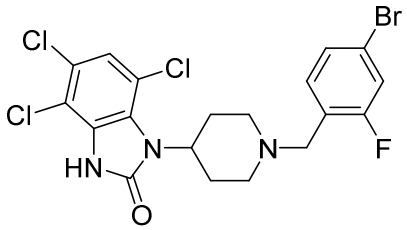
5,6-Dichloro-1-(1-(4-bromo-2-fluorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**44**)[8]



This compound was prepared according to the procedure for compound **2** in 31% yield from 5,6-dichloro-1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-

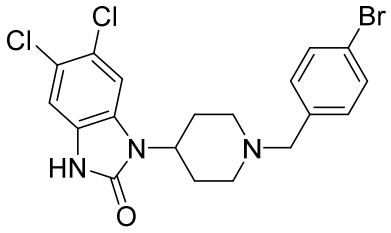
one. Methane sulfonic acid (13 μL, 0.2 mmol) was added to a suspension of **44** in EtOH (1 mL). The mixture was heated to 60 ^{o}C for 30 min. The solvent was removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was frozen and then subjected to lyophilization overnight giving product **44** in the form of a mesylate salt. ^{1}H NMR mesylate (400 MHz, CD_3OD) δ 7.61 (dd, *J* = 9.0, 1.4 Hz, 1H), 7.56 (dd, *J* = 4.0, 2.0 Hz, 2H), 7.47 (s, 1H), 7.20 (s, 1H), 4.53 (tt, *J* = 12.4, 4.0 Hz, 1H), 4.45 (s, 2H), 3.70 (d, *J* = 12.8 Hz, 2H), 3.35-3.28 (m, 2H), 2.81-2.71 (m, 5H), 2.09 (d, *J* = 14.4 Hz, 2H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{18}BrCl_2FN_3O$ is 471.99, found 472.18; HPLC t_R = 4.00 min.

4,5,7-Trichloro-1-(1-(4-bromo-2-fluorobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**45**)



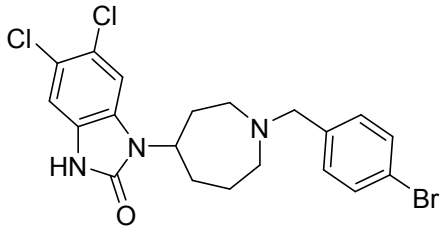
This compound was prepared according to the procedure for compound **17** in 34% yield from 4,5,7-trichloro-1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. A solution of methane sulfonic acid in EtOH (0.06 M, 1.0 mL, 0.06 mmol) was added to **45**. The solvent was removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was frozen and then subjected to lyophilization overnight giving product **45** in the form of a mesylate salt. ^{1}H NMR mesylate (400 MHz, CD_3OD) δ 7.57-7.53 (m, 3H), 7.42 (s, 1H), 4.36 (s, 2H), 3.79 (tt, *J* = 11.4, 4.4 Hz, 1H), 3.57 (d, *J* = 12.8 Hz, 2H), 3.14 (td, *J* = 13.0, 2.2 Hz, 2H), 2.72 (s, 3H), 2.20 (d, *J* = 14.4 Hz, 2H), 1.87 (qd, *J* = 13.8, 3.6 Hz, 2H); MS(*m/z*): [M + H] calc'd for $C_{19}H_{17}BrCl_3FN_3O$ is 505.95, found 505.77; HPLC t_R = 4.51 min.

5,6-Dichloro-1-(1-(4-bromobenzyl)piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**46**)[2,8]



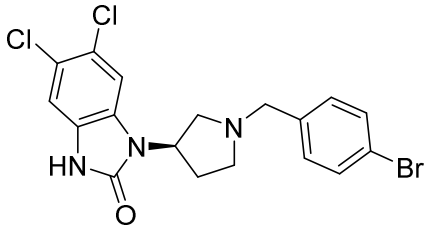
This compound was prepared according to the procedure for compound **17** in 42% yield from 5,6-dichloro-1-(piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. Methane sulfonic acid (13 μL, 0.2 mmol) was added to a suspension of **46** in EtOH (1 mL). The mixture was heated to 60 ^{o}C for 30 min. The solvent was removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was frozen and then subjected to lyophilization overnight giving product **46** in the form of a mesylate salt. ^{1}H NMR mesylate (400 MHz, CD_3OD) δ 7.71 (dd, *J* = 6.6, 1.6 Hz, 2H), 7.50 (dd, *J* = 6.6, 1.6 Hz, 2H), 7.48 (s, 1H), 7.19 (s, 1H), 4.52 (tt, *J* = 12.4, 4.0 Hz, 1H), 4.37 (s, 2H), 3.63 (d, *J* = 12.8 Hz, 2H), 3.25 (td, *J* = 13.0, 2.4 Hz, 2H), 2.80-2.69 (m, 5H), 2.08 (d, *J* = 14.8 Hz, 2H); MS(*m/z*): [M + H] calc'd for $C_{19}H_{19}BrCl_2N_3O$ is 454.00, found 454.23; HPLC t_R = 3.76 min.

5,6-Dichloro-1-(1-(4-bromobenzyl)azepan-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**47**)



This compound was prepared according to the procedure for compound **4** in 71% yield from 5,6-dichloro-1-(azepan-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. A solution of methane sulfonic acid in EtOH (0.06 M, 1.0 mL, 0.06 mmol) was added to **47**. The solvent was removed under reduced pressure and the residue was dissolved in 1:1 water/acetonitrile. The solution was frozen and then subjected to lyophilization overnight giving product **47** in the form of a mesylate salt. ^{1}H NMR mesylate (400 MHz, CD_3OD) δ 7.67 (d, *J* = 1.6 Hz, 2H), 7.49 (t, *J* = 8.0 Hz, 3H), 7.19 (s, 1H), 4.58-4.51 (m, 1H), 4.40 (s, 2H), 3.66-3.61 (m, 1H), 3.43 (m, 3H), 2.78-2.70 (m, 4H), 2.38-2.30 (m, 1H), 2.23-2.09 (m, 3H), 2.04-2.02 (m, 1H); MS(*m/z*): [M+H] calc'd for $C_{20}H_{21}BrCl_2N_3O$ is 468.02, found 468.05; HPLC t_R = 3.87 min.

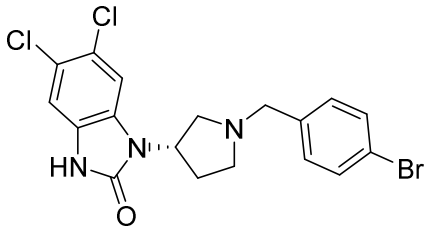
(*R*)-5,6-dichloro-1-(1-(4-bromobenzyl)pyrrolidin-3-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, **(48**)



This compound was prepared according to the procedure for compound **9** in 62% yield from (*R*)-5,6-dichloro-1-(pyrrolidin-3-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.19 (s, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.12 (s, 1H), 5.16-5.12 (m, 1H), 3.76 (d, *J* = 12.8 Hz, 1H), 3.50 (d, *J* = 12.8 Hz, 1H), 3.24 (t, *J* = 8.0 Hz, 1H), 2.96 (d, *J* = 10.0 Hz, 1H), 2.51 (t, *J* =

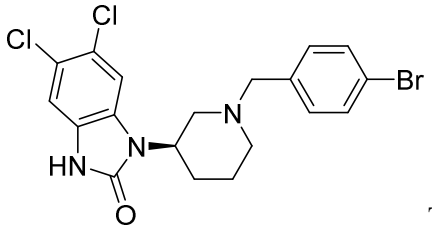
10.0 Hz, 1H), 2.37-2.25 (m, 2H), 2.04 (t, J = 9.8 Hz, 1H); MS(*m/z*): [M+H] calc'd for $C_{18}H_{17}BrCl_2N_3O$ is 439.99, found 439.96; HPLC t_R = 4.26 min.

(*S*)-5,6-dichloro-1-(1-(4-bromobenzyl)pyrrolidin-3-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**49**)



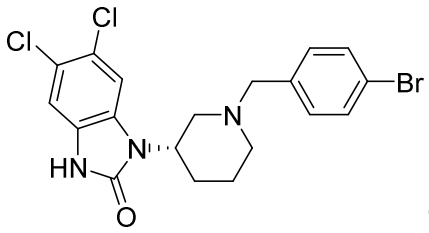
This compound was prepared according to the procedure for compound **9** in 61% yield from (*S*)-5,6-dichloro-1-(pyrrolidin-3-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (s, 1H), 8.19 (s, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.15 (s, 1H), 5.15 (tt, J = 10.4, 3.6 Hz, 1H), 3.76 (d, J = 12.8 Hz, 1H), 3.51 (d, J = 12.8 Hz, 1H), 3.25 (t, J = 12.4 Hz, 1H), 2.96 (d, J = 10.4 Hz, 1H), 2.52 (t, J = 9.6 Hz, 1H), 2.37-2.26 (m, 2H), 2.08-1.98 (m, 1H); MS(*m/z*): [M+H] calc'd for $C_{18}H_{16}BrCl_2N_3O$ is 439.99, found 439.99; HPLC t_R = 3.29 min.

(*R*)-1-(1-(4-bromobenzyl)piperidin-3-yl)-5,6-dichloro-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**50**)



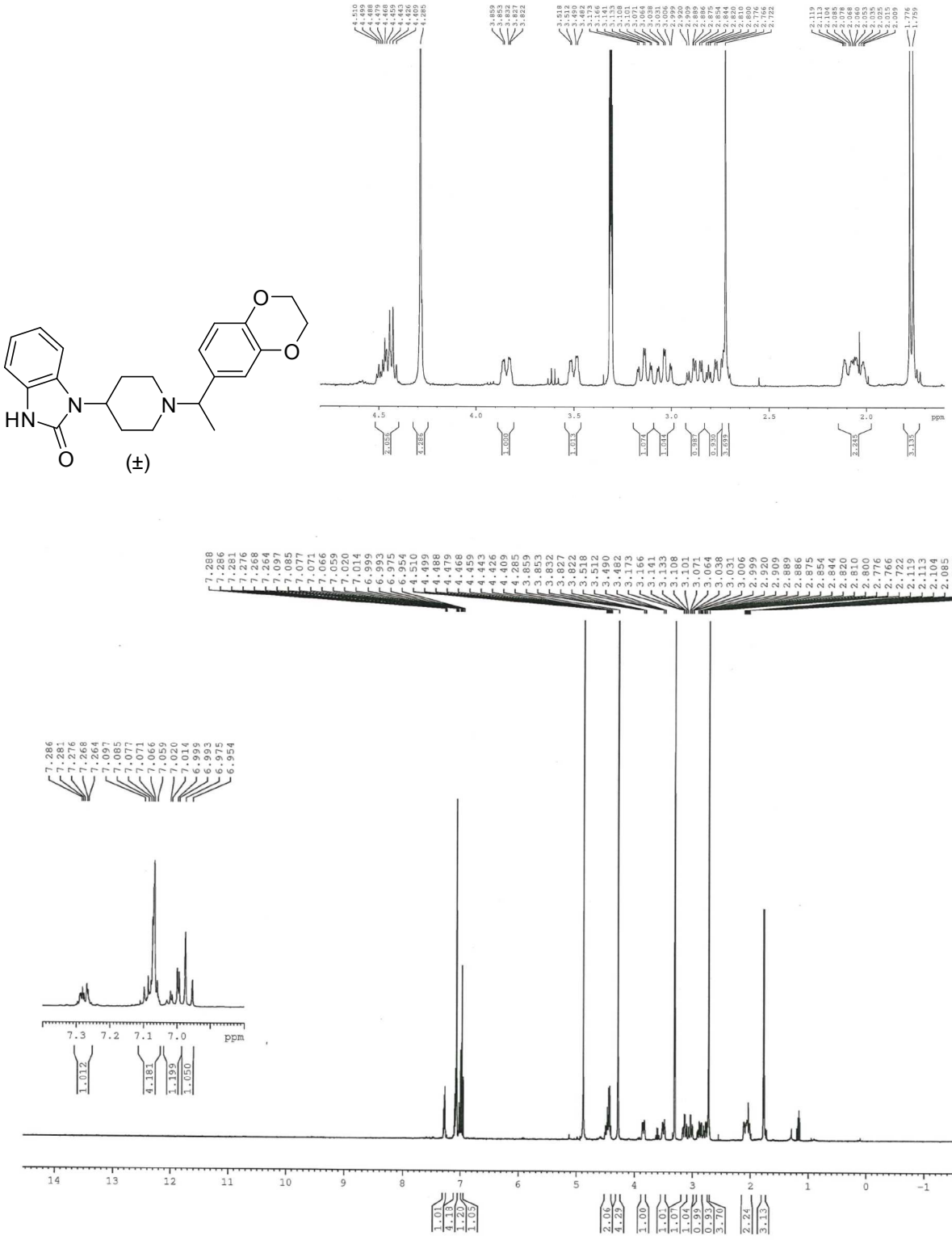
This compound was prepared according to the procedure for compound **9** in 36% yield from (*R*)-5,6-dichloro-1-(piperidin-3-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. ^{1}H NMR (400 MHz, CD_3OD) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.44 (s, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.16 (s, 1H), 4.38 (tt, *J* = 11.6, 4.0 Hz, 1H), 3.59 (s, 2H), 2.90 (d, *J* = 11.2 Hz, 2H), 2.74 (t, *J* = 10.6 Hz, 1H), 2.26-2.16 (m, 2H), 1.87 (dd, *J* = 11.6, 2.2 Hz, 2H), 1.79-1.78 (m, 1H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{19}BrCl_2N_3O$ is 454.00, found 454.04; HPLC t_R = 4.24 min.

(*S*)-1-(1-(4-bromobenzyl)piperidin-3-yl)-5,6-dichloro-1*H*-benzo[*d*]imidazol-2(3*H*)-one, (**51**)

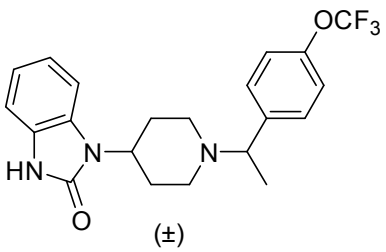


This compound was prepared according to the procedure for compound **9** in 42% yield from (*S*)-5,6-dichloro-1-(piperidin-3-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one. ^{1}H NMR (400 MHz, CD_3OD) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.43 (s, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.16 (s, 1H), 4.38 (tt, *J* = 12.0, 3.8 Hz, 1H), 3.59 (s, 2H), 2.90 (d, *J* = 11.6 Hz, 2H), 2.74 (t, *J* = 11.0 Hz, 1H), 2.26-2.12 (m, 2H), 1.87 (dd, *J* = 12.2, 2.2 Hz, 2H), 1.79-1.69 (m, 1H); MS(*m/z*): [M+H] calc'd for $C_{19}H_{19}BrCl_2N_3O$ is 454.00, found 454.00; HPLC t_R = 4.14 min.

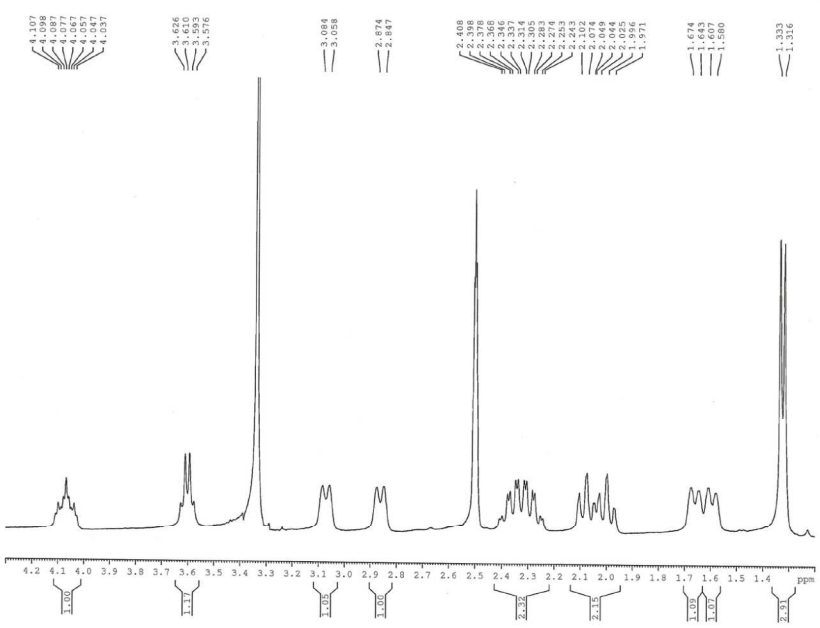
^{1} HNMR of (**25**)

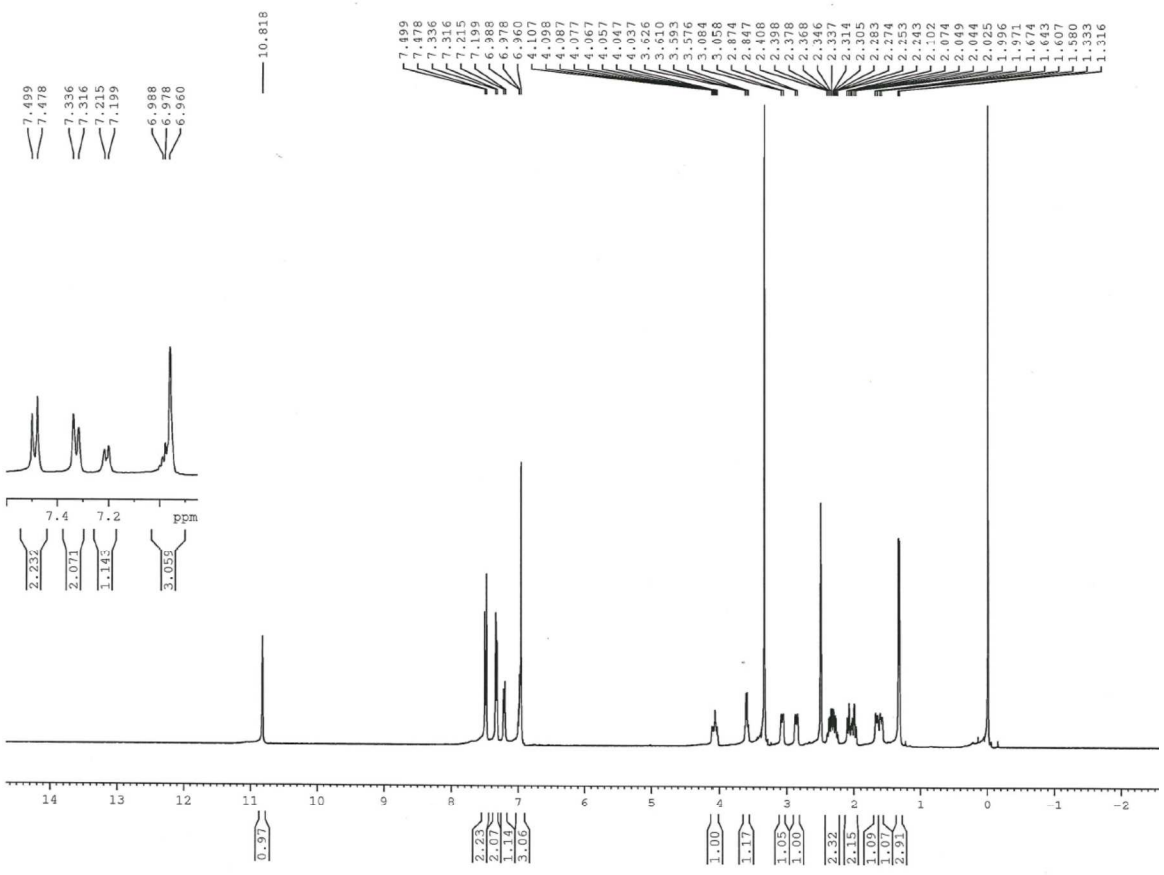


[1] HNMR of (**26**)

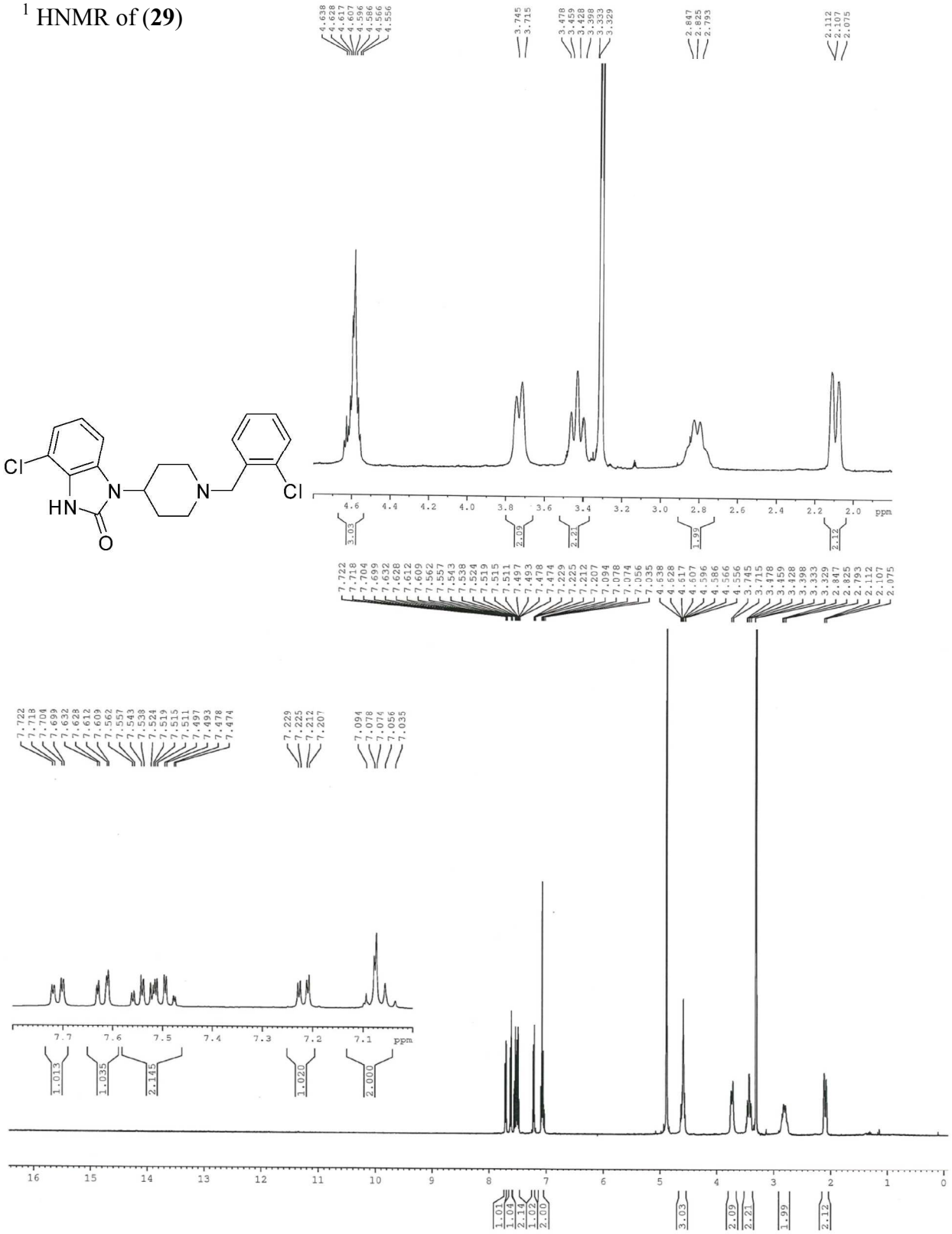


(±)





[1] HNMR of (**29**)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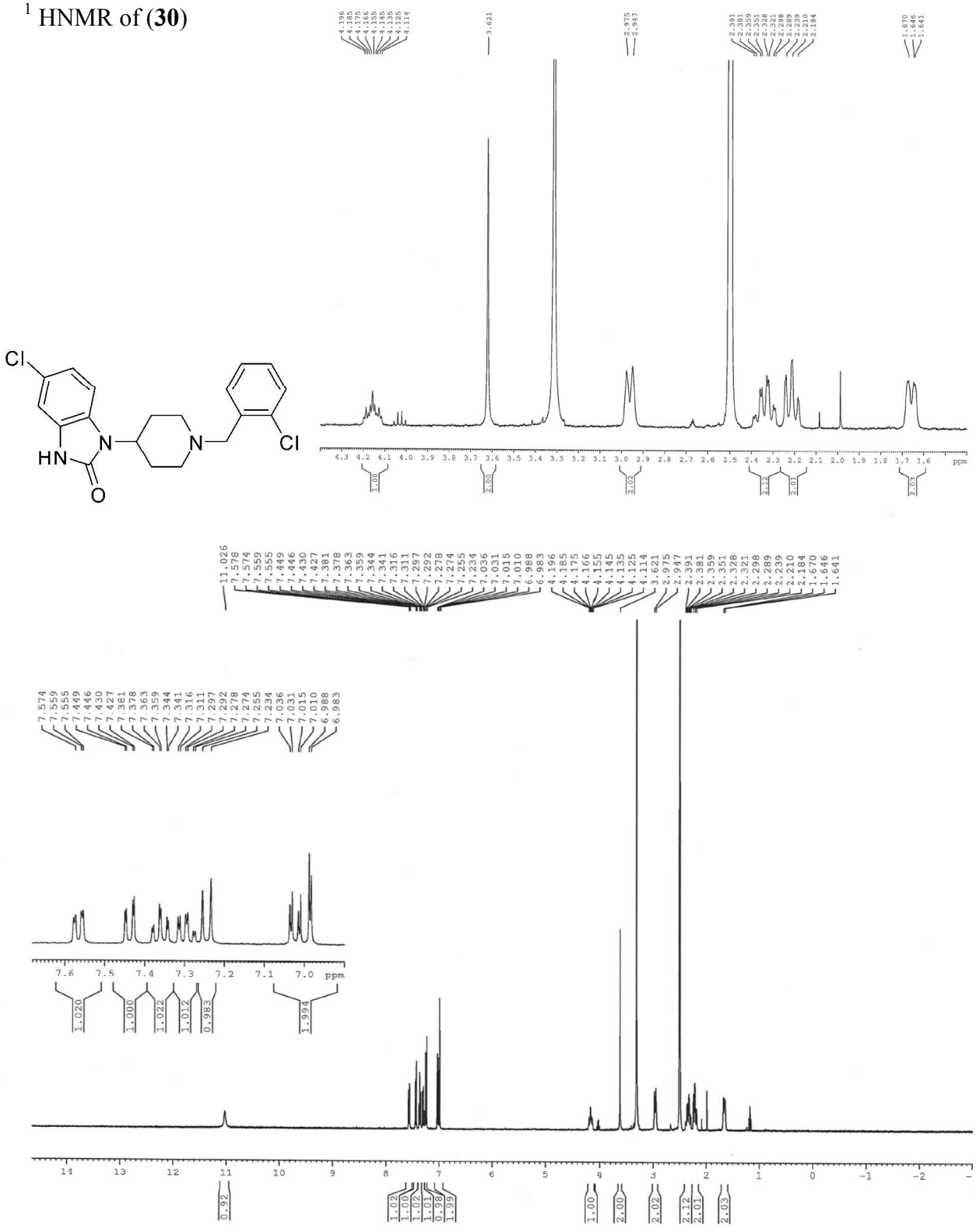
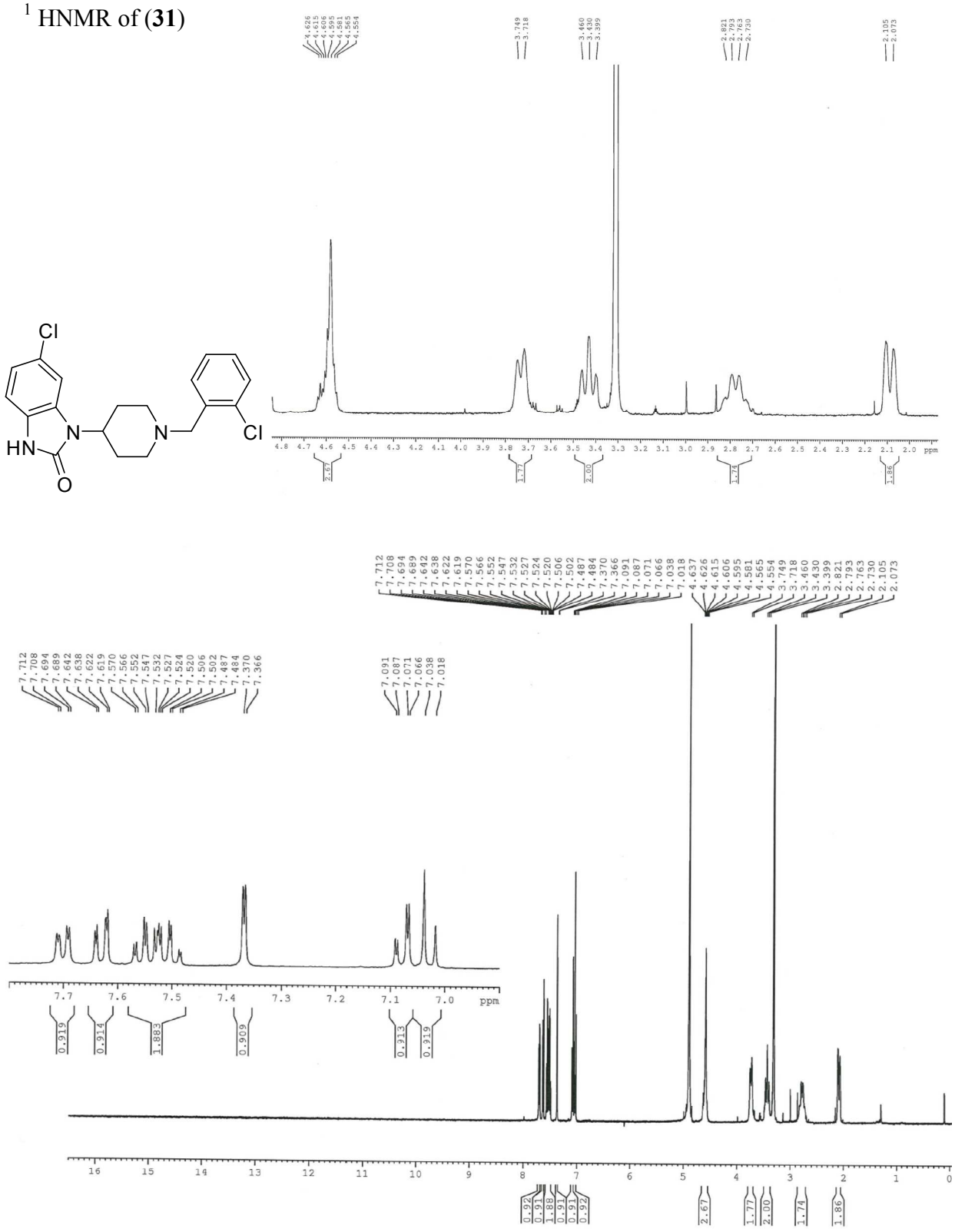
2.14
1.02
2.00

[1] HNMR of (**30**)



[1] HNMR of (**31**)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7.552
7.547
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7.520
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7.370
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7.087
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7.066
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2.073
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0.914
1.883
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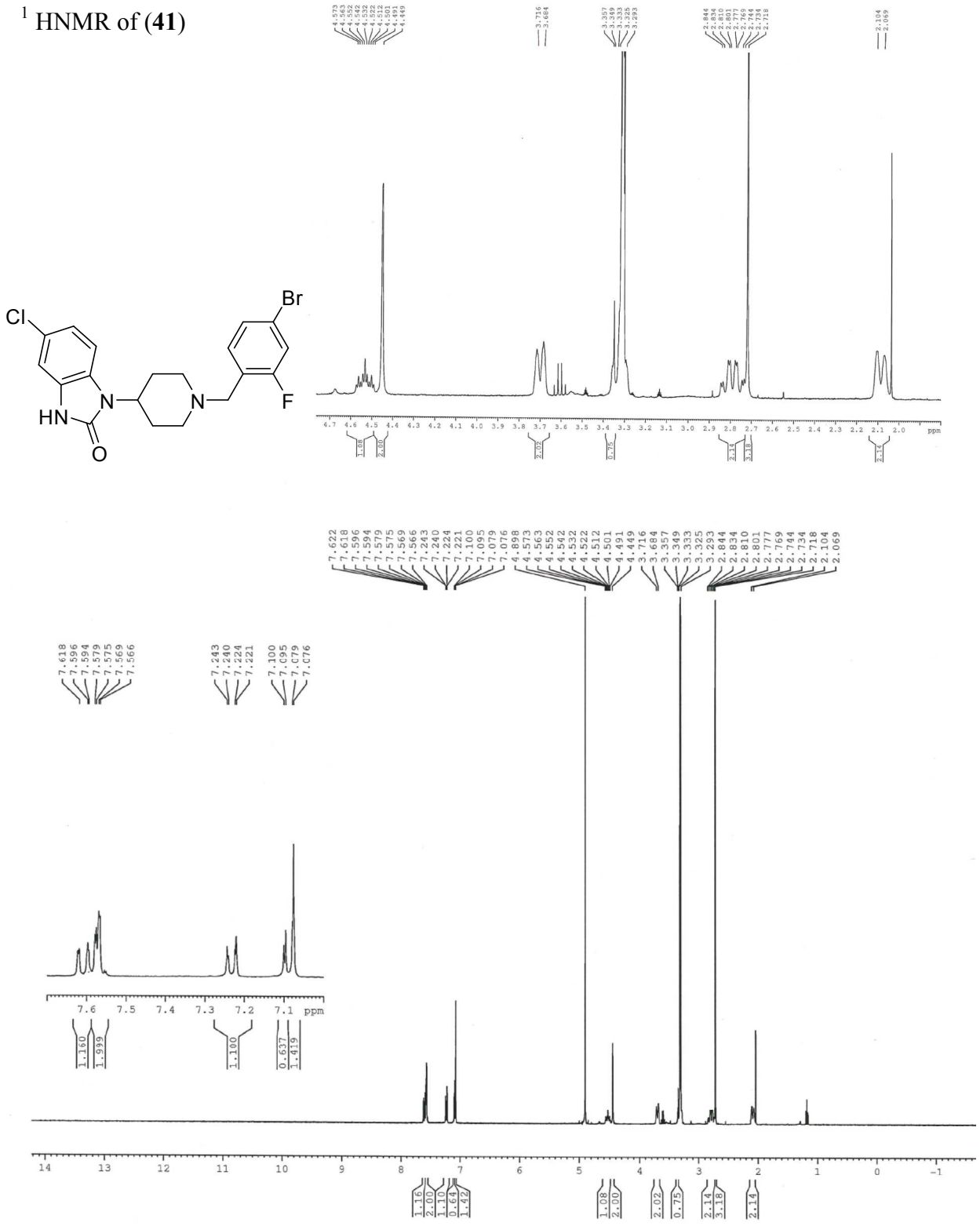
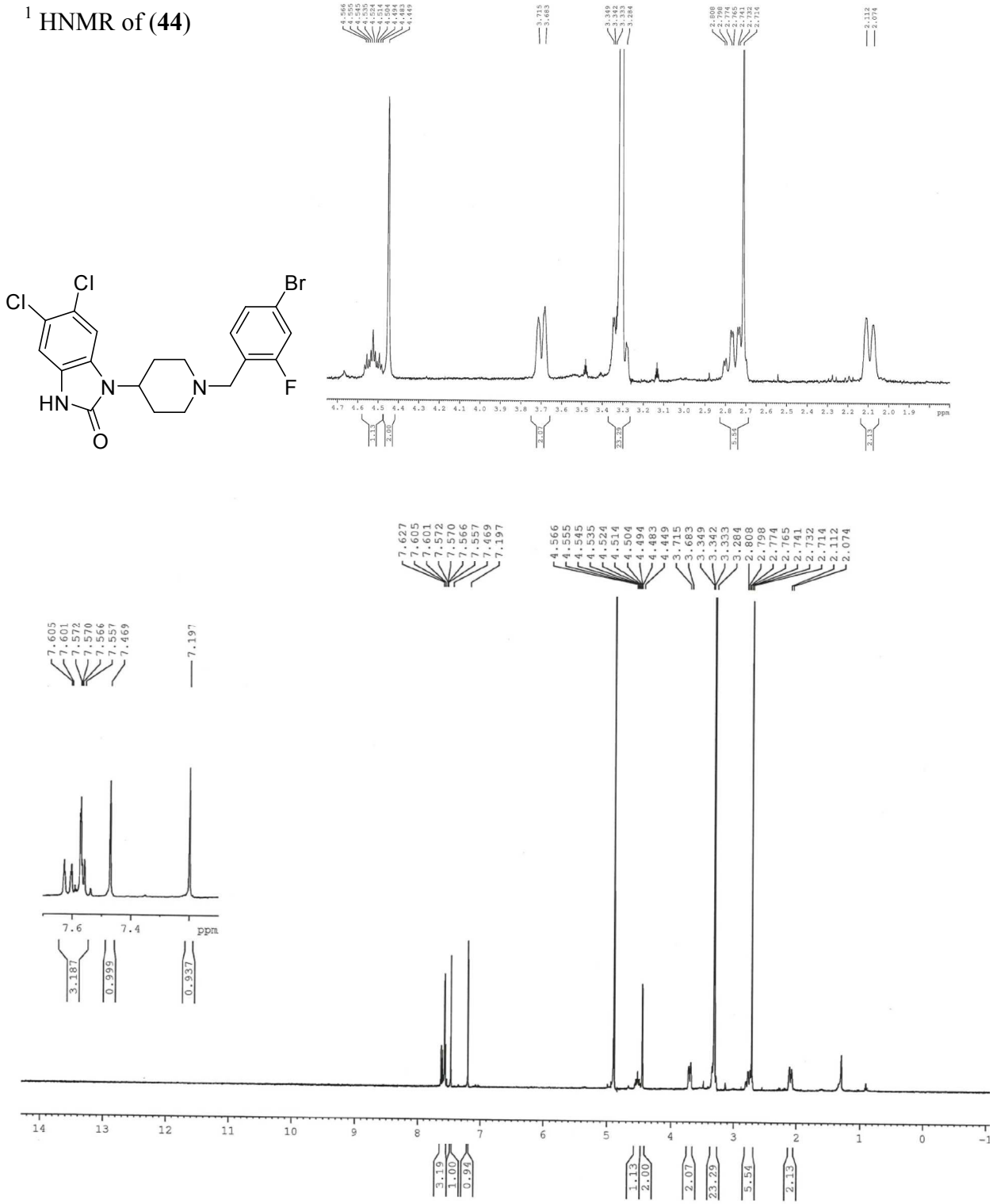
2.00
1.74
1.86

[1] HNMR of (**41**)



[1] HNMR of (**44**)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7.469
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ppm
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1.00
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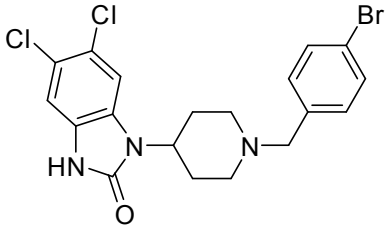
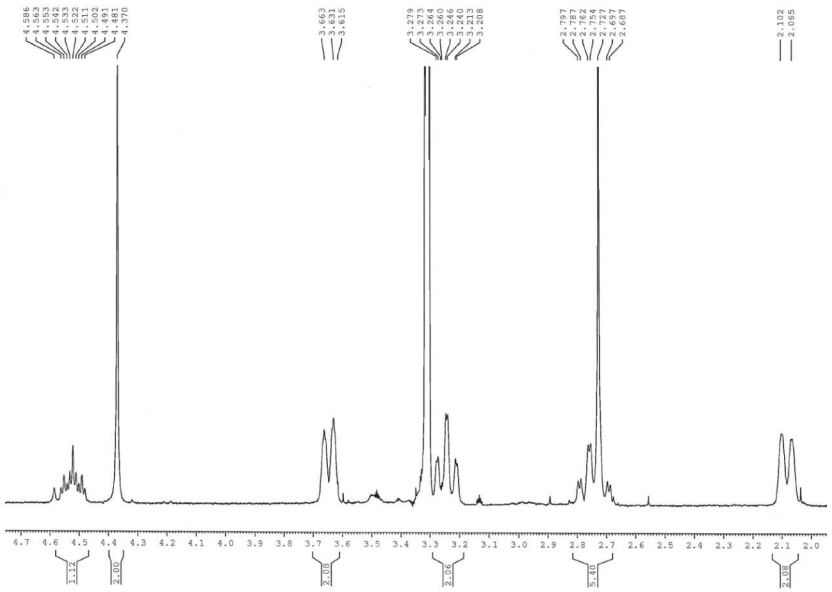
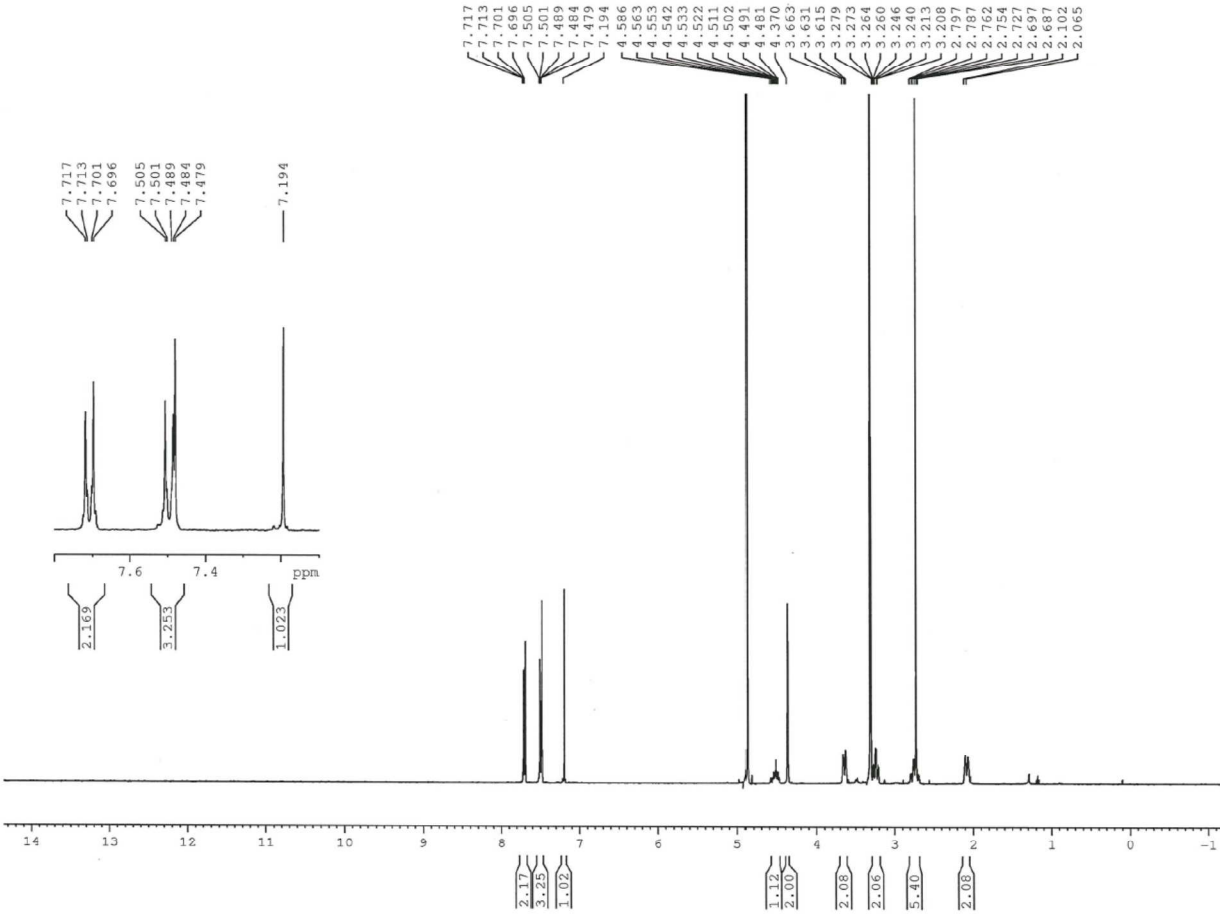
0.937

[1] HNMR of (**46**)







Molecular Strings

Compound	Smiles
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3	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC(Cl)=CC=C4)CC3
4	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC=C(Cl)C=C4)CC3
5	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC=C(C)C=C4)CC3
6	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC=C(Br)C=C4)CC3
7	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC=C(OC)C=C4)CC3
8	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC=C(NC(C)=O)C=C4)CC3
9	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC=C(C#N)C=C4)CC3
10	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC=C(C(N)=O)C=C4)CC3
11	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC(OC)=CC=C4)CC3
12	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC(OC(F)(F)F)=CC=C4)CC3
13	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=CC(Cl)=C(Cl)C=C4)CC3
14	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=C(C)C=C(Cl)C=C4)CC3
15	O=C1NC2=C(C=CC=C2)N1C3CCN(CC4=C(F)C=C(Br)C=C4)CC3
16	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=CC=CC=C4)CC3
17	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=C(Cl)C=CC=C4)CC3
18	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=CC=C(Cl)C=C4)CC3
19	O=C1NC2=C(C=CC=C2)N1C3CCN(C(CC)C4=CC=C(Cl)C=C4)CC3
20	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=CC=C(F)C=C4)CC3
21	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=CC=C(Br)C=C4)CC3
22	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=CC=C(OC)C=C4)CC3
23	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=CC=C(OCC)C=C4)CC3
24	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=CC=C(OC(C)C)C=C4)CC3
25	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=CC(OCCO5)=C5C=C4)CC3

26	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=CC=C(OC(F)(F)F)C=C4)CC3
27	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=C(F)C=C(Br)C=C4)CC3
28	O=C1NC2=C(C=CC=C2)N1C3CCN(C(C)C4=C(F)C=C(Cl)C=C4)CC3
29	O=C1NC2=C(C=CC=C2Cl)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
30	O=C1NC2=C(C=CC(Cl)=C2)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
31	O=C1NC2=C(C=C(Cl)C=C2)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
32	O=C1NC2=C(C(Cl)=CC=C2)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
33	O=C1NC2=C(C=CC(C)=C2)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
34	O=C1NC2=C(C=CC(Br)=C2)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
35	O=C1NC2=C(C=CC(F)=C2)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
36	O=C1NC2=C(C=CC(OC)=C2)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
37	O=C1NC2=C(C=CC(OC(F)(F)F)=C2)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
38	O=C1NC2=C(C=CC(S(=O)(C)=O)=C2)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
39	O=C1NC2=C(C=CC(C#N)=C2)N1C3CCN(CC4=C(Cl)C=CC=C4)CC3
40	O=C1NC2=C(C=CC=C2Cl)N1C3CCN(CC4=C(F)C=C(Br)C=C4)CC3
41	O=C1NC2=C(C=CC(Cl)=C2)N1C3CCN(CC4=C(F)C=C(Br)C=C4)CC3
42	O=C1NC2=C(C=C(Cl)C=C2)N1C3CCN(CC4=C(F)C=C(Br)C=C4)CC3
43	O=C1NC2=C(C=C(Cl)C=C2Cl)N1C3CCN(CC4=C(F)C=C(Br)C=C4)CC3
44	O=C1NC2=C(C=C(Cl)C(Cl)=C2)N1C3CCN(CC4=C(F)C=C(Br)C=C4)CC3
45	O=C1NC2=C(C(Cl)=CC(Cl)=C2Cl)N1C3CCN(CC4=C(F)C=C(Br)C=C4)CC3
46	O=C1NC2=C(C=C(Cl)C(Cl)=C2)N1C3CCN(CC4=CC=C(Br)C=C4)CC3
47	O=C1NC2=C(C=C(Cl)C(Cl)=C2)N1C3CCN(CC4=CC=C(Br)C=C4)CCC3
48	O=C1NC2=C(C=C(Cl)C(Cl)=C2)N1[C@@H]3CCN(CC4=CC=C(Br)C=C4)C3
49	O=C1NC2=C(C=C(Cl)C(Cl)=C2)N1[C@H]3CCN(CC4=CC=C(Br)C=C4)C3
50	O=C1NC2=C(C=C(Cl)C(Cl)=C2)N1[C@@H]3CCCN(CC4=CC=C(Br)C=C4)C3
51	O=C1NC2=C(C=C(Cl)C(Cl)=C2)N1[C@H]3CCCN(CC4=CC=C(Br)C=C4)C3

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