Supporting Information

for

Synthesis and Evaluation of Novel Ligustrazine Derivatives as Multi-Targeted Inhibitors for the Treatment of Alzheimer's Disease

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$^1$H NMR (300 MHz, CDCl$_3$) of 8a

$^{13}$C NMR (75 MHz, CDCl$_3$) of 8a
HRMS spectra of 8a
$^{1}$H NMR (300 MHz, CDCl$_3$) of 8b

$^{13}$C NMR (75 MHz, CDCl$_3$) of 8b
HRMS spectra of 8b
$^1$H NMR (300 MHz, CDCl$_3$) of 8c

$^{13}$C NMR (75 MHz, CDCl$_3$) of 8c
HRMS spectra of 8e
$^1$H NMR (400 MHz, DMSO-d6) of 8d

$^{13}$C NMR (100 MHz, DMSO-d6) of 8d
HRMS spectra of 8d
$^1$H NMR (300 MHz, CDCl$_3$) of 8e

$^{13}$C NMR (75 MHz, CDCl$_3$) of 8e
HRMS spectra of 8e
$^1$H NMR (300 MHz, CDCl₃) of 8f

$^{13}$C NMR (75 MHz, CDCl₃) of 8f
HRMS spectra of 8f

### Data File: 120170411-02V23.jpg

| Element | Vol | Min | Max | Total | Error Margin (ppm) | DBE Range | Electron Loss | Use Adduct |
|---------|-----|-----|-----|-------|-------------------|----------|--------------|-----------|
| H       | 1   | 0   | 60  | 0     | 20                | -2.0 - 1000.0 | both         | Na        |
| B       | 3   | 0   | 0   | 0     | unlimited         | apply N Rule: yes | Use MSn info: iso |
| C       | 4   | 0   | 50  | 0     | 75.00             | 75.00     | AND         | Max Results: 500 |

### Results

- **Element:** H, B, C
- **Vol:** 1, 3, 4
- **Min:** 0, 0, 0
- **Max:** 60, 0, 50
- **Total:** 0, 0, 0
- **Error Margin (ppm):** 20
- **DBE Range:** -2.0 - 1000.0
- **Electron Loss:** both
- **Use Adduct:** Na
- **MSn Logic Mode:** AND
- **Max Results:** 500

#### Measured region for 385.0936 m/z

- **Peak:** 385.0936
- **Intensity:** 100.0

#### Predicted region for 385.0926 m/z

- **Peak:** 385.0926
- **Intensity:** 100.0

### Rank

| Rank | Score | Formula (M)   | Ion     | Meas. m/z | Pred. m/z | mDa | ppm | DEE |
|------|-------|---------------|---------|-----------|-----------|-----|-----|-----|
| 2    | 8.3   | C18 H19 N2 O4 Cl | [M+Na]⁺ | 385.0936  | 385.0925  | 1.0 | 0.0 | 10.0 |

### Diagrams

1. HRMS spectra showing peaks at various m/z values.
2. Measured region for 385.0936 m/z.
3. Predicted region for 385.0926 m/z.
$^1$H NMR (400 MHz, DMSO-d6) of 8g

$^{13}$C NMR (100 MHz, DMSO-d6) of 8g
HRMS spectra of 8g

Data File: 12070411-GY1.txt

| Elmt | Val | Min | Max | Elmt | Val | Min | Max | Elmt | Val | Min | Max | Use Adduct |
|------|-----|-----|-----|------|-----|-----|-----|------|-----|-----|-----|------------|
| N    | 1   | 0   | 50  | O    | 2   | 0   | 6   | P    | 3   | 0   | 6   | H          |
|      | C   | 4   | 0   | S    | 1   | 1   | 0   | Br   | 2   | 0   | 0   | Co         |
|      | N   | 0   | 5   | Si   | 1   | 1   | 0   | I    | 0   | 0   | 0   | H          |

Error Margin (ppm): 100
DDE Range: -2.0 - 1000.0
Electron loss: both
HC Ratio: unlimited
Apply N Rule: yes
Max Isotopes: 11
Isotope IM (%) : 1.00
Used MSn Info: no
Isotope R(%) : 10000
Max Results: 500

Event#: 1 MS[+H]+, Ret. Time: 1.249 - 1.507 - 1.793, Scan id: 187 - 227 - 269

Measured region for 407.0605 m/z

C18 H18 N2 O4 Br [M-H]-: Predicted region for 407.0601 m/z

Rank | Score | Formula (M) | Ion | Meas m/z | Pred m/z | Df (mDa) | Df (ppm) | Ipe | DBR
--- | ----- | ----------- | ---- | -------- | -------- | -------- | -------- |---- |----
2   | 72.39 | C18 H19 N2 O4 Br | [M-H]^- | 407.0605 | 407.0601 | 0.4     | 0.98    | 72.38 | 13.0
$^1$H NMR (400 MHz, DMSO-d6) of 8h

$^{13}$C NMR (100 MHz, DMSO-d6) of 8h
HRMS spectra of 8h
$^1$H NMR (400 MHz, DMSO-d6) of 8i

$^{13}$C NMR (100 MHz, DMSO-d6) of 8i
HRMS spectra of 8i
$^1$H NMR (400 MHz, DMSO-d6) of 8j

$^{13}$C NMR (100 MHz, DMSO-d6) of 8j
HRMS spectra of 8j
$^{1}H$ NMR (400 MHz, DMSO-d$_6$) of 8k

$^{13}$C NMR (100 MHz, DMSO-d$_6$) of 8k
HRMS spectra of 8k

Measured region for 369.1231 m/z

C18H19N2 O4 F (M+Na)+ Predicted region for 369.1221 m/z

Rank | Score | Formula (M) | ion | Meas. m/z | Pred. m/z | Dr. (mDa) | Dr. (ppm) | Iso | DBE
--- | --- | --- | --- | --- | --- | --- | --- | --- | ---
1 | 83.70 | C18 H19 N2 O4 F | [M+Na]+ | 369.1231 | 369.1221 | 1.0 | 27.10 | 87.40 | 10.0
$^1$H NMR (300 MHz, CDCl$_3$) of 81

$^{13}$C NMR (75 MHz, CDCl$_3$) of 81
HRMS spectra of $8l$

Formula Predictor Report - 19.tcd

| Elmt | Vol | Min | Max |
|------|-----|-----|-----|
| H    | 1   | 0   | 50  |
| O    | 2   | 0   | 7   |
| P    | 3   | 0   | 0   |
| Cu   | 2   | 0   | 0   |
| Br   | 1   | 0   | 0   |
| Na   | 3   | 0   | 0   |
| C    | 4   | 0   | 50  |
| F    | 1   | 0   | 1   |
| Cl   | 1   | 0   | 0   |
| I    | 3   | 0   | 0   |

Error Margin (ppm): 20
DBE Range: -2.0 - 1000.0

Measured region for 455.1783 m/z:

C22 H28 N2 O7 $[M+Na]^-$: Predicted region for 455.1789 m/z:

Ranks:

| Rank | Score | Formula (M) | Ion | Meas. m/z | Pred. m/z | Df (mDa) | Df (ppm) | Ion DBE |
|------|-------|-------------|-----|-----------|-----------|----------|----------|---------|
| 3    | 69.47 | C22 H28 N2 O7 | $[M+Na]^-$ | 455.1783 | 455.1789 | -6.6 | -1.32 | 70.93 | 10.0 |
$^1$H NMR (400 MHz, DMSO-d6) of 8m

$^{13}$C NMR (100 MHz, DMSO-d6) of 8m
HRMS spectra of 8m
$^1$H NMR (400 MHz, DMSO-d6) of 8n

$^{13}$C NMR (100 MHz, DMSO-d6) of 8n
HRMS spectra of 8n
$^1$H NMR (400 MHz, DMSO-d6) of 8o

$^{13}$C NMR (100 MHz, DMSO-d6) of 8o
HRMS spectra of $80$
$^{1}H$ NMR (400 MHz, DMSO-d6) of $8p$

$^{13}C$ NMR (100 MHz, DMSO-d6) of $8p$
HRMS spectra of 8p
$^1$H NMR (300 MHz, CDCl$_3$) of 8q

$^{13}$C NMR (75 MHz, CDCl$_3$) of 8q
HRMS spectra of 8q
$^1$H NMR (300 MHz, CDCl$_3$) of 8r

$^{13}$C NMR (300 MHz, CDCl$_3$) of 8r
HRMS spectra of $8r$

| Element | Val | Min | Max | Use Adduct |
|---------|-----|-----|-----|------------|
| H       | 1   | 0   | 60  |            |
| O       | 2   | 0   | 7   |            |
| P       | 3   | 0   | 0   |            |
| Cu      | 2   | 0   | 0   |            |
| Br      | 1   | 0   | 0   |            |
| Na      |     |     |     |            |
| C       | 4   | 0   | 55  |            |
| Cl      | 1   | 0   | 0   |            |
| Ni      | 2   | 0   | 0   |            |

Error Margin (ppm): 20  
DBE Range: -20 - 1000.0  
Electron Ions: both

Max Isotope (all) Isotope RI (%): 75.08
MSn Logic Mode: AND

Measured region for 352.1271 m/z

C17 H19 N3 O4 [M+Na]⁺ - Predicted region for 352.1268 m/z

| Rank | Score | Formula (M) | Ions | Meas. m/z | Pred. m/z | Dif. (mDa) | Dif. (ppm) | ioe | DBE |
|------|-------|-------------|------|-----------|-----------|------------|------------|-----|-----|
| 1    | 86.72 | C17 H19 N3 O4 | [M+Na]⁺ | 352.1271  | 352.1268  | 0.3        | 0.85       | 86.72| 19.0 |