Synthesis of benzimidazole based 1,3,4-oxadiazole-1,2,3-triazole conjugates as glycogen synthase kinase-3β inhibitors with antidepressant activity in in vivo models.

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Dose-response curves of compounds 7q, 7b, 7e and 7n for GSK-3β assays.

Results are presented as the percentage of GSK-3β inhibition in the presence of the tested compounds. Data are the mean ± SEM of n = 2.
Spectral characterization of representative compounds:

$1-((5-((1-(2-fluorophenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole$

(7b)
Carbon-13 NMR – 7b
7b- Expanded

Carbon-13 NMR – 7b (Expanded)
ESI-MS – 7b

-ESI Scan:2 (0.2-0.3 min, 9 Scans) Frag=135.0V BOT2.d

Counts vs. Mass-to-Charge (m/z)

+ESI Scan:1 (0.1-0.3 min, 9 Scans) Frag=135.0V BOT2.d

Counts vs. Mass-to-Charge (m/z)
1-((5-((1-(3-chlorophenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7d)

Proton NMR – 7d
Carbon-13 NMR – 7d
Carbon-13 NMR – 7d (Expanded)
ESI-MS – 7d
1-((5-((1-(2-bromophenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole

(7f)
Carbon-13 NMR – 7f
1-((5-((1-(2-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7k)

Proton NMR – 7k
Carbon NMR – 7k
Carbon NMR – 7k (Expanded)
1-((5-((1-(4-fluorophenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7a)
$1-((5-((1-(2-chlorophenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole$ (7c)
1-((5-((1-phenyl-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7e)
1-(((5-((1-(2-chloropyridin-3-yl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7g)
1-((5-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7h)
Sample code; -7h; m/z=487

Event#: 1 Q1 Scan(E+) Ret. Time: [0.327->0.336]-[0.150<->0.433] Scan#: [75->77]-[35<->99]

7h
1-((5-((1-(3,4-dichlorophenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7i)
Event#: 1 Q1 Scan(E+) Ret. Time: [0.874->0.883]-[0.627<->0.919] Scan#: [199->201]-[143<->209]
1-((5-((1-(2,4-dichlorophenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7j)
1-((5-((1-(4-tert-butylphenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7l)
Event#: 1 Q1 Scan(E+) Ret. Time : [0.327->0.336]-[0.150<>0.433] Scan# : [75->77]-[35<>99]
$1-((5-((1-o-tolyl-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole$ (7m)
1-((5-((1-(4-ethylphenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7n)
1-((5-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7o)
Analysis Report

Sample Information:
- Sample Name: BOT15
- Sample ID: BOT15
- Data Filename: BOT15_001.lcd
- Method Filename: general.ldm
- Batch Filename: 22062014 MS.ldb
- Vial #: 1-99
- Injection Volume: 0.4 uL
- Date Acquired: 22-06-2014 12:09:52
- Date Processed: 22-06-2014 12:10:53
- Sample Type: Unknown
- Acquired by: System Administrator
- Processed by: System Administrator

MS Spectrum

Positive Line: R. Time: (Scan #: 1)
- MassPeaks: 98
- Spectrum Mode: Averaged 0.168-0.186 (39-43) Base Peak: 492 (108370)
- BG Mode: Calc Segment 1 - Event 1

Negative Line: R. Time: (Scan #: 2)
- MassPeaks: 98
- Spectrum Mode: Averaged 0.181-0.199 (42-46) Base Peak: 274 (218157)
- BG Mode: Calc Segment 1 - Event 2

m/z
1-((5-((1-(3,4-dimethylphenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7p)
Event#: 1 Q1 Scan(E+)  Ret. Time : [0.680->0.689]-[0.486<->0.724]  Scan# : [155->157]-[111<->165]
1-((5-((1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7q)
1-((1-(3-nitrophenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzod[d]imidazole (7r)
1-((5-((1-(3-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl)methyl)-2-(trifluoromethyl)-1H-benzo[d]imidazole (7s)
4-(4-((5-((2-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)-1,3,4-oxadiazol-2-ylthio)methyl)-1H-1,2,3-triazol-1-yl)benzonitrile (7t)