FIG. 1A

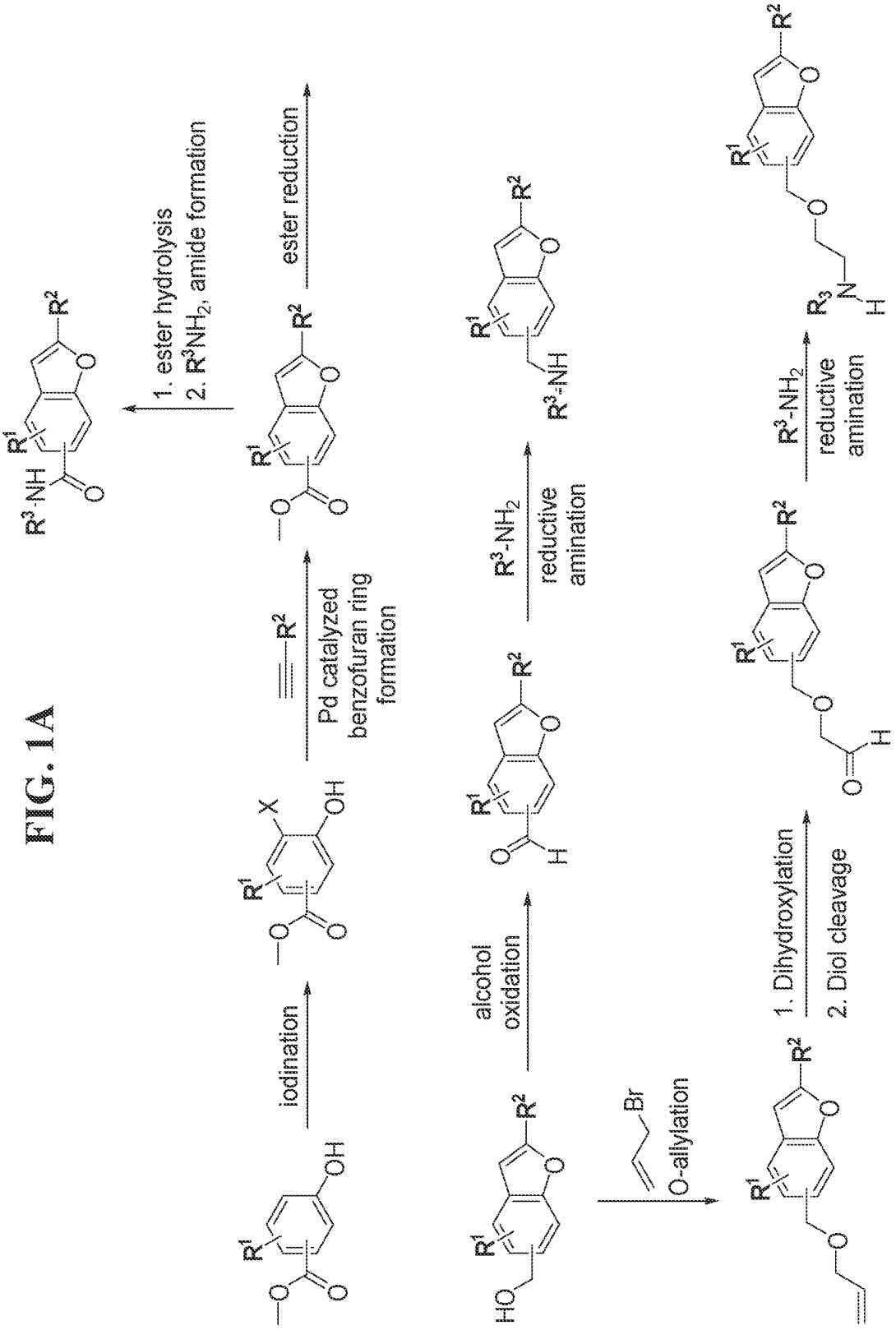

1. ester hydrolysis
2. R3NH2, amide formation
ester reduction
Pd catalyzed benzofuran ring formation
iodination
alcohol oxidation
R3-NH2 reductive amination
O-allylation
1. Dihydroxylation
2. Diol cleavage
R3-NH2 reductive amination

FIG. 1B

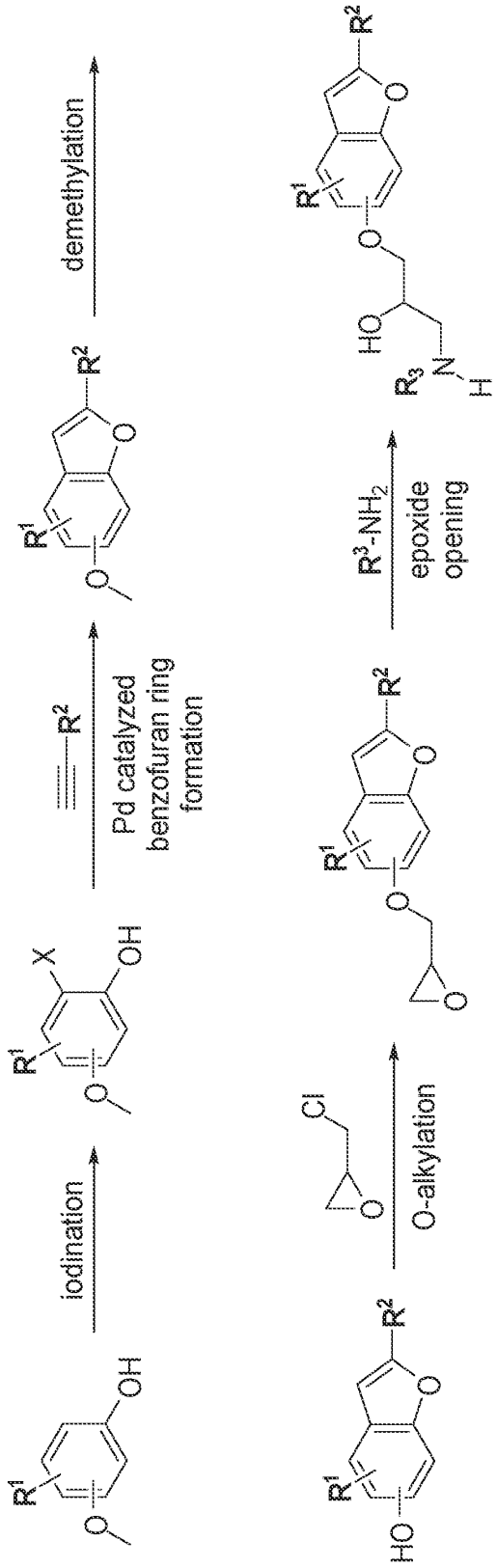

iodination
Pd catalyzed benzofuran ring formation
demethylation
O-alkylation
epoxide opening
R^3-NH_2

FIG. 1C

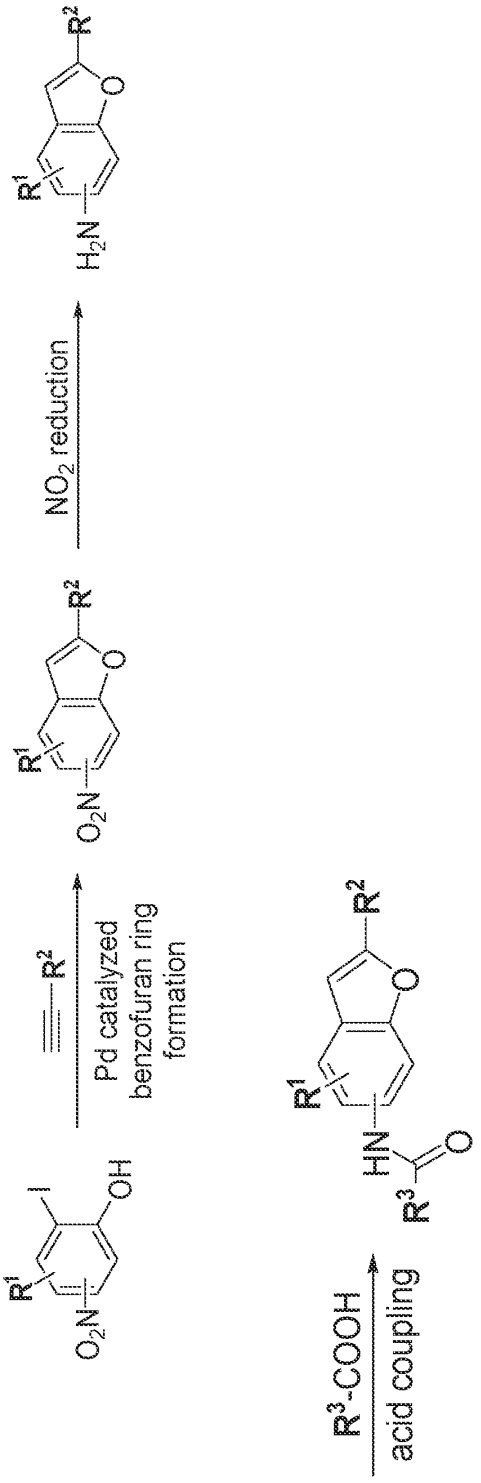
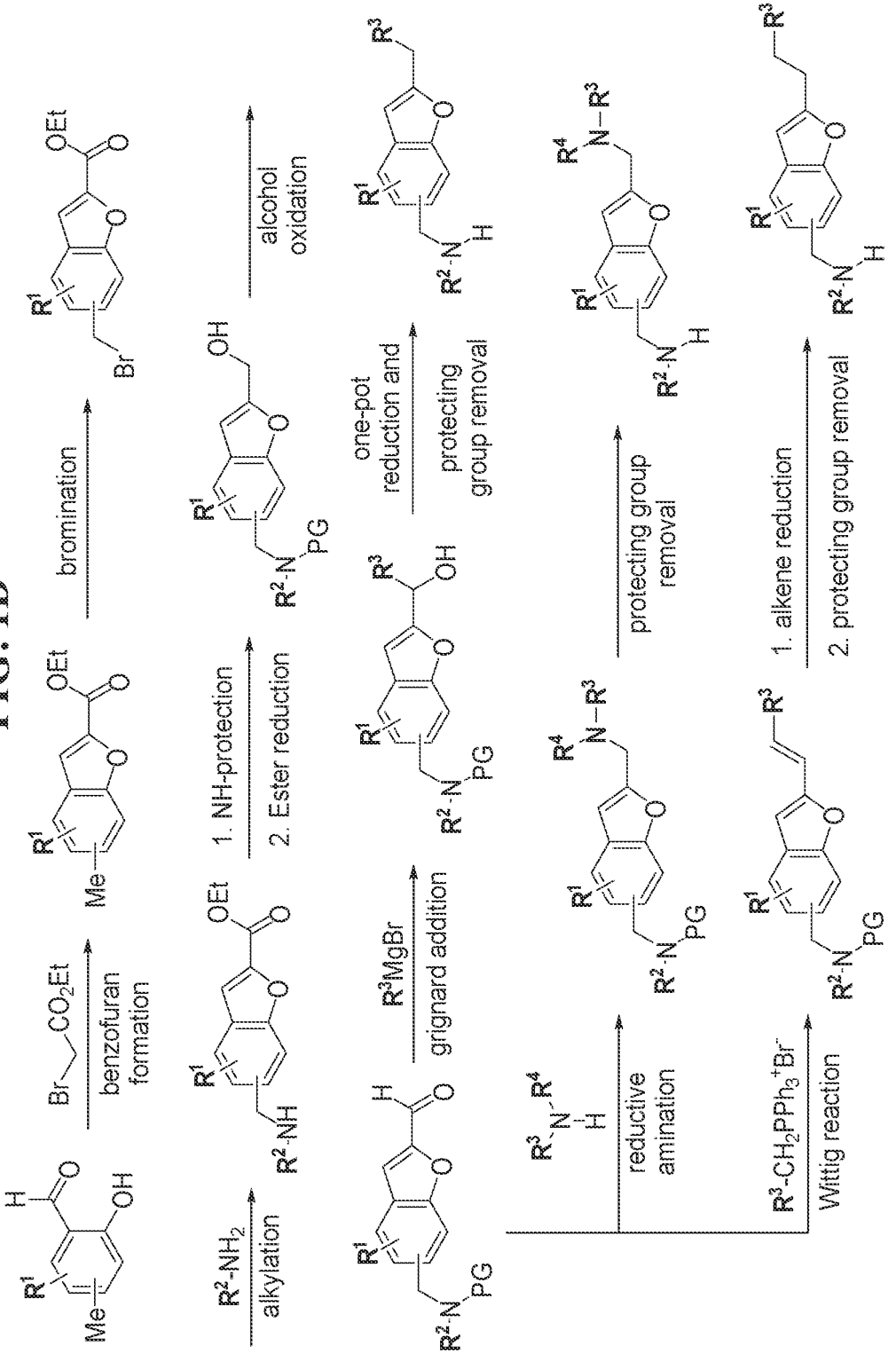

R3-COOH
acid coupling
Pd catalyzed
benzofuran ring
formation
NO2 reduction

FIG. 1D


benzofuran formation
bromination
1. NH-protection
2. Ester reduction
alcohol oxidation
alkylation
grignard addition
one-pot reduction and
protecting group removal
reductive amination
protecting group removal
Wittig reaction
1. alkene reduction
2. protecting group removal

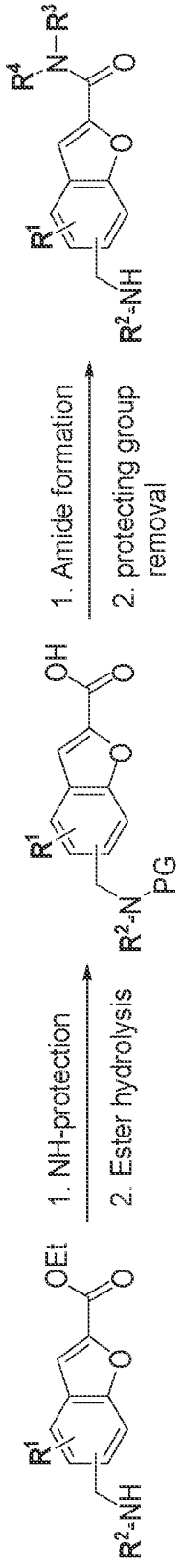

OEt
O
O
R1
R2-NH
1. NH-protection
2. Ester hydrolysis
OH
O
O
R1
R2-N
PG
1. Amide formation
2. protecting group removal
R4
N
R3
O
O
R1
R2-NH

FIG. 1D (cont.)

FIG. 1E

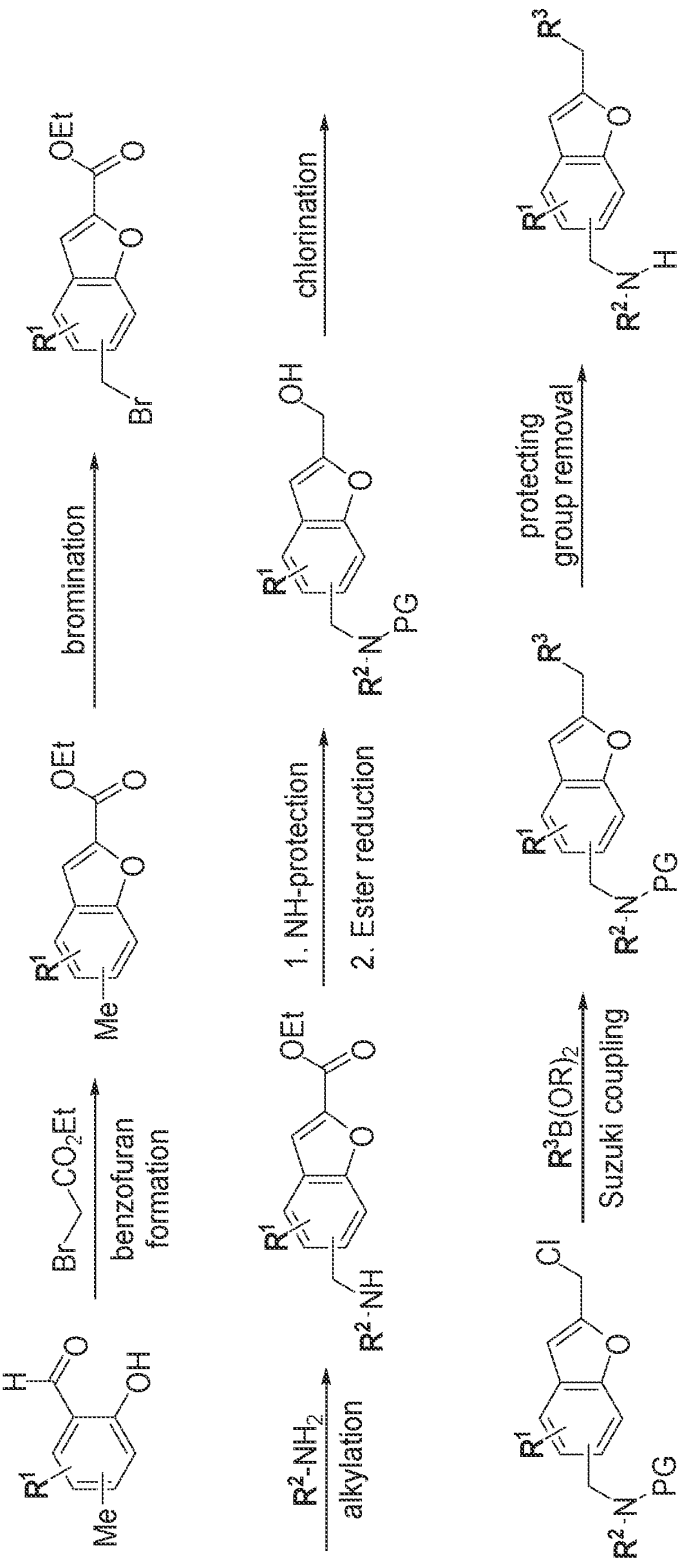

benzofuran formation
bromination
chlorination
1. NH-protection
2. Ester reduction
protecting group removal
alkylation
Suzuki coupling

FIG. 1F

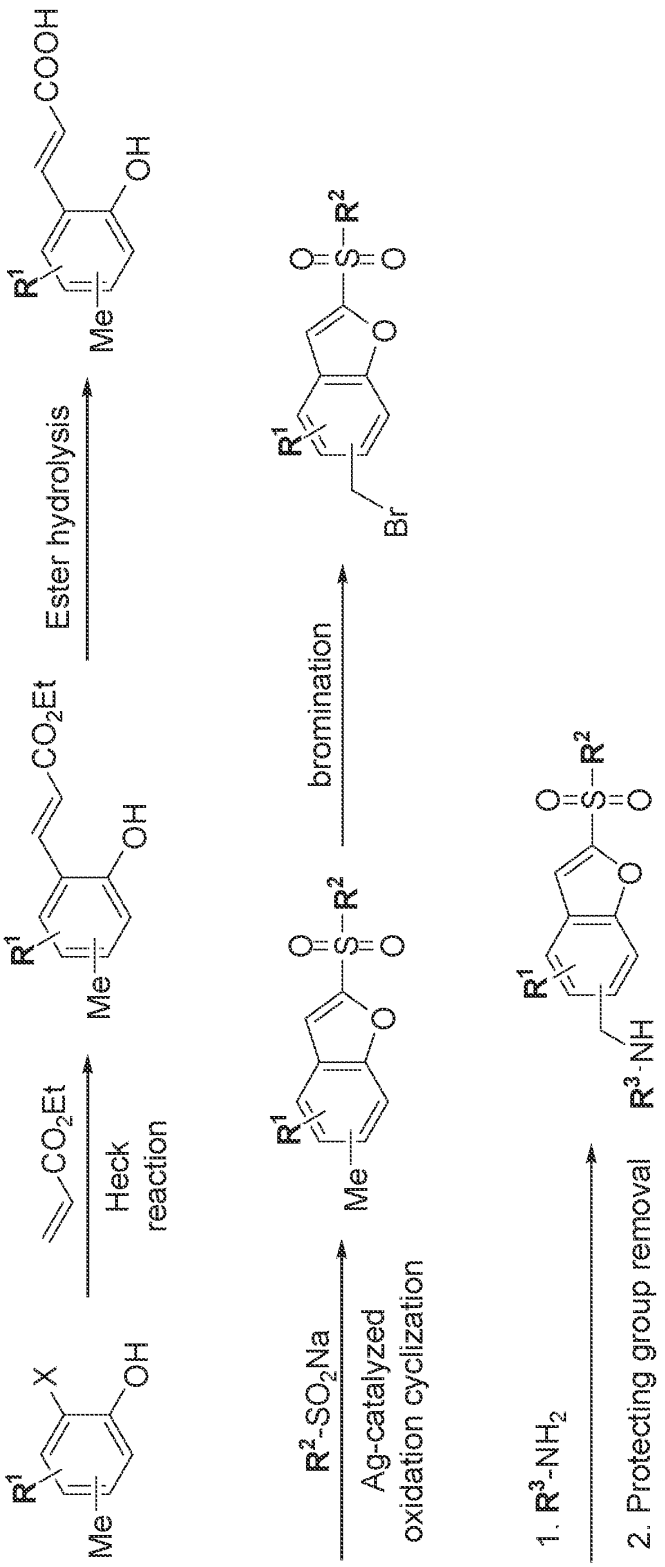

Heck reaction
Ester hydrolysis
bromination
Ag-catalyzed oxidation cyclization
1. R3-NH2
2. Protecting group removal

FIG. 1G

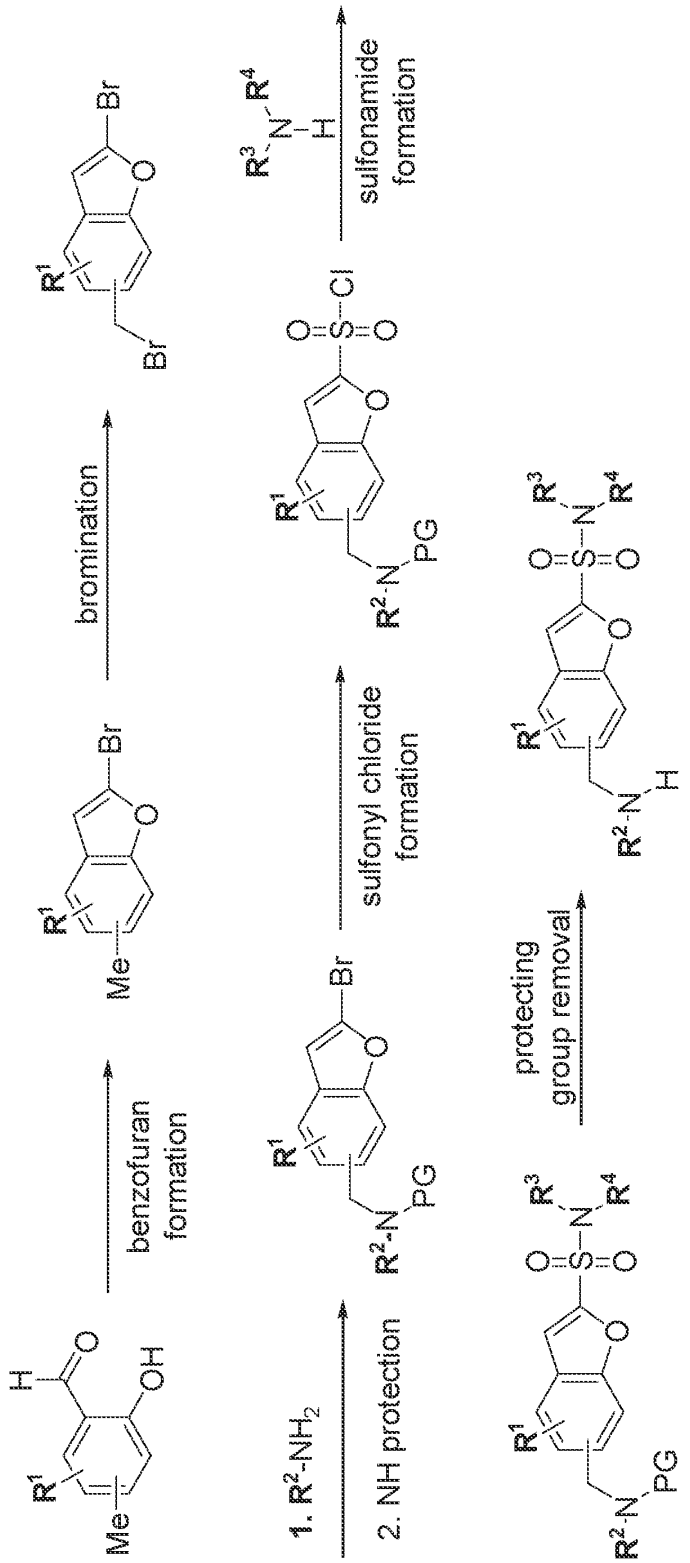

benzofuran formation
bromination
1. R2-NH2
2. NH protection
sulfonyl chloride formation
sulfonamide formation
protecting group removal

FIG. 1H

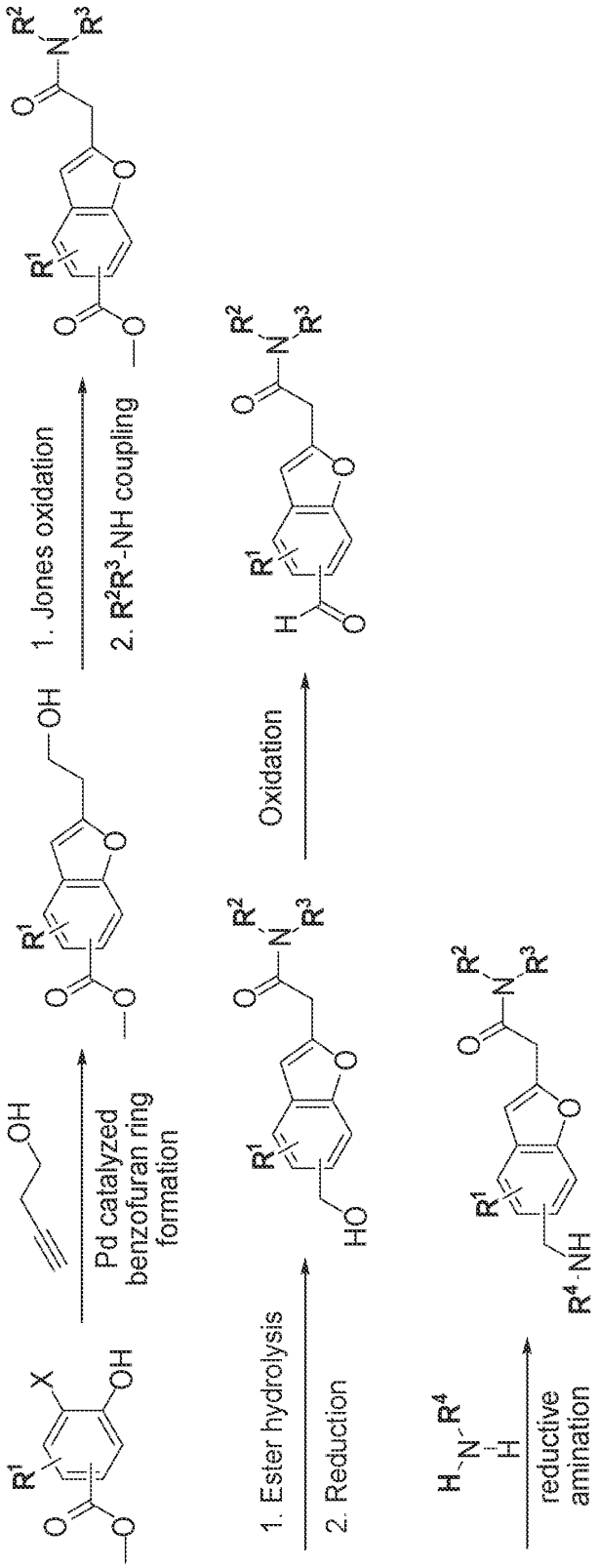

Pd catalyzed benzofuran ring formation
1. Ester hydrolysis
2. Reduction
Oxidation
1. Jones oxidation
2. R2R3-NH coupling
reductive amination

FIG. 1I

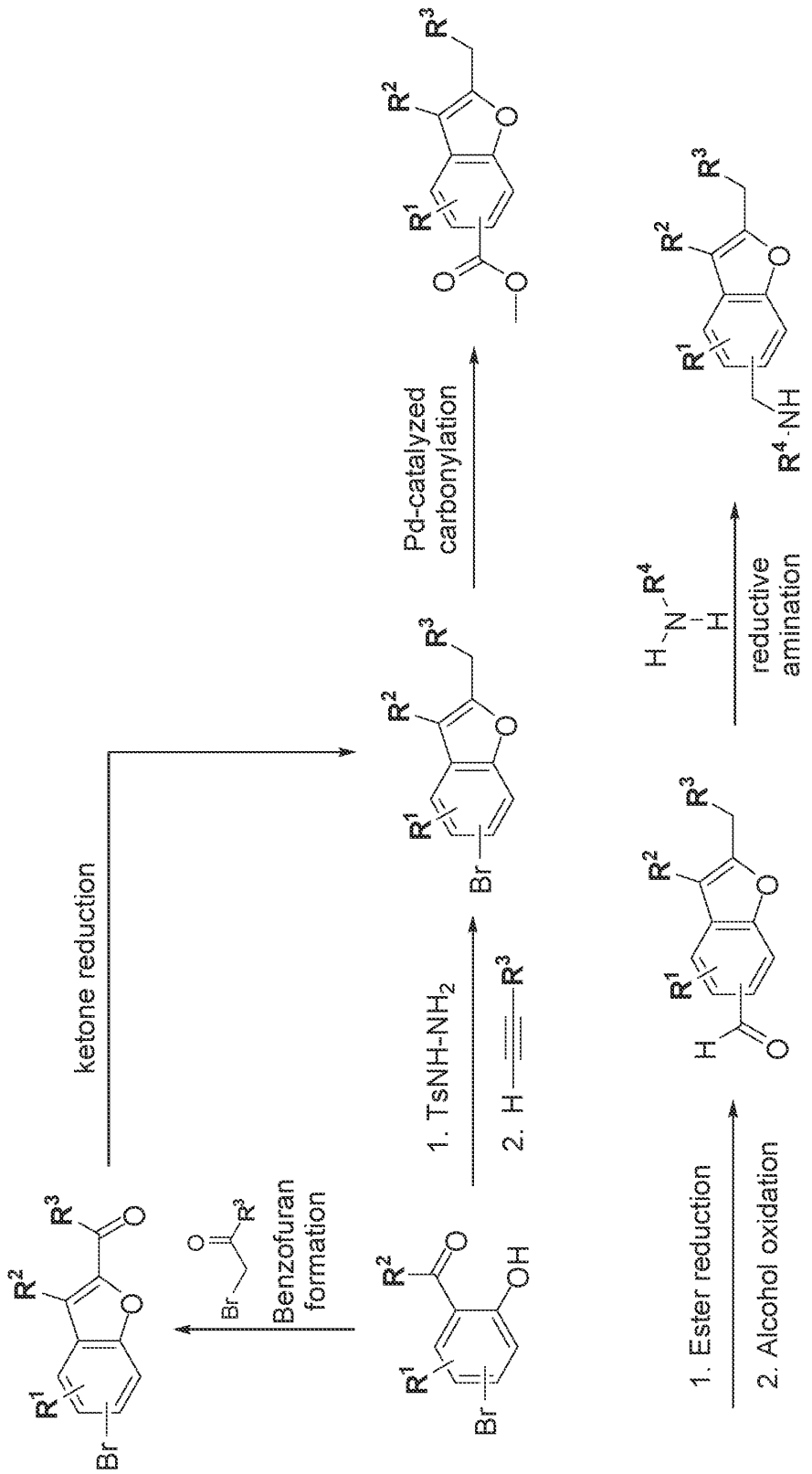

ketone reduction
Benzofuran formation
1. TsNH-NH2
2. H
Pd-catalyzed carbonylation
1. Ester reduction
2. Alcohol oxidation
reductive amination
R1
R2
R3
R4
Br
OH
O
H
N

FIG. 1J

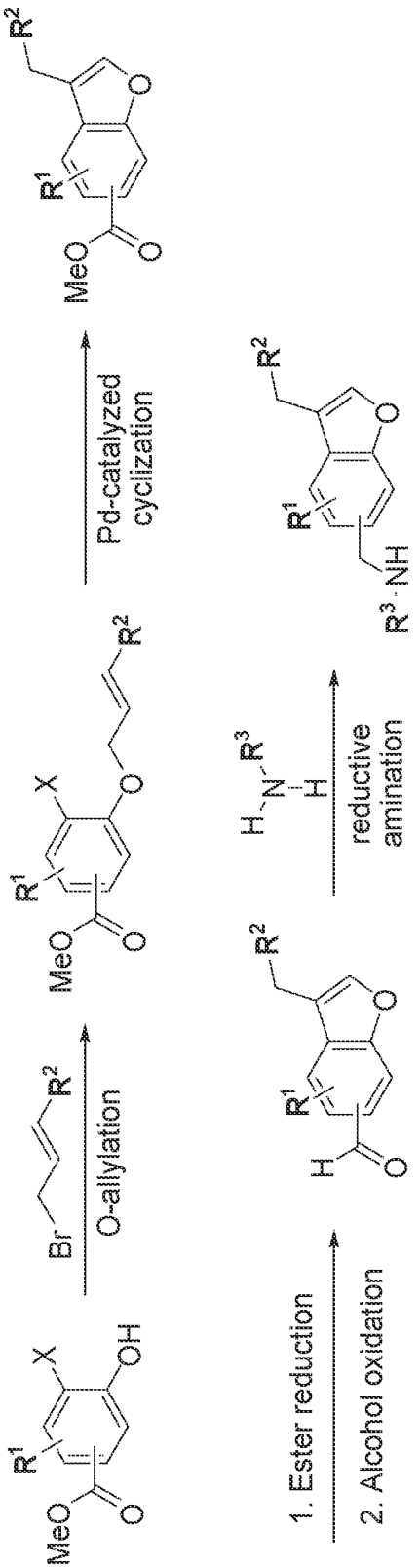

MeO
O
R1
X
OH
Br
R2
O-allylation
MeO
O
R1
X
O
R2
Pd-catalyzed cyclization
MeO
O
R1
O
R2
1. Ester reduction
2. Alcohol oxidation
H
O
R1
O
R2
H
N
R3
H
reductive amination
R3
NH
R1
O
R2

FIG. 1K

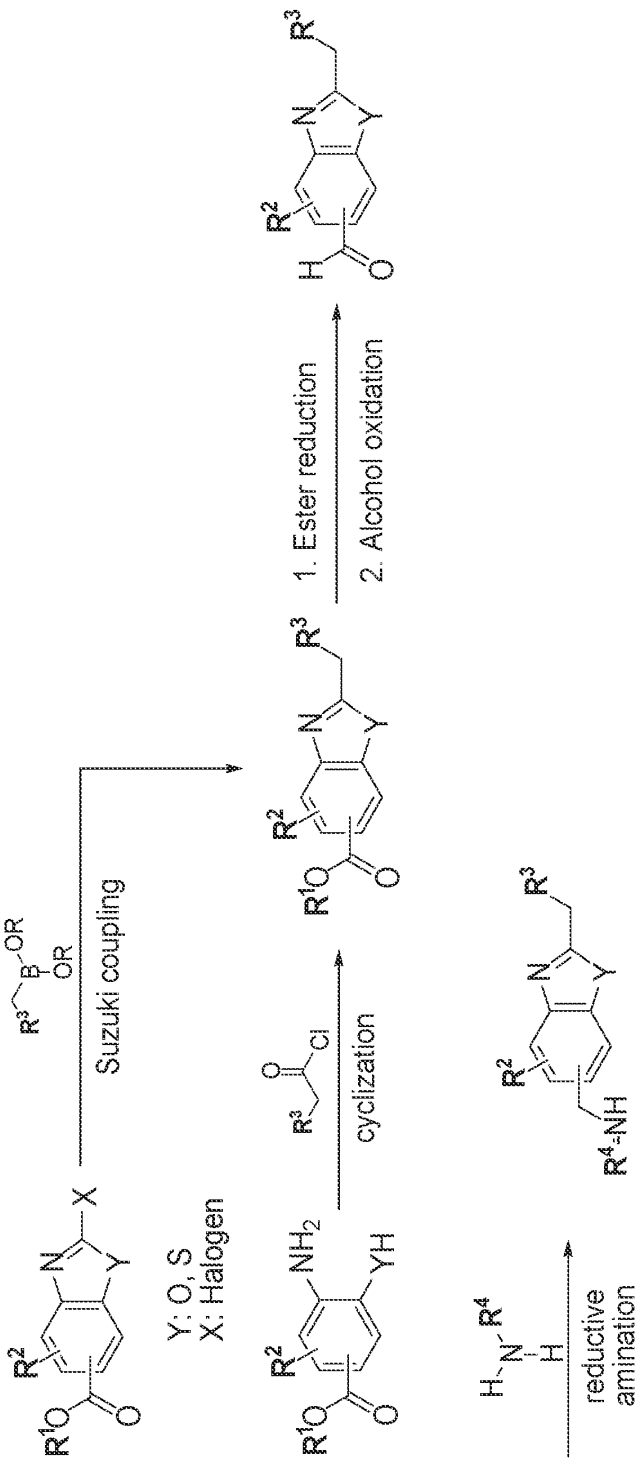

Suzuki coupling
Y: O, S
X: Halogen
cyclization
1. Ester reduction
2. Alcohol oxidation
reductive amination

FIG. 1L

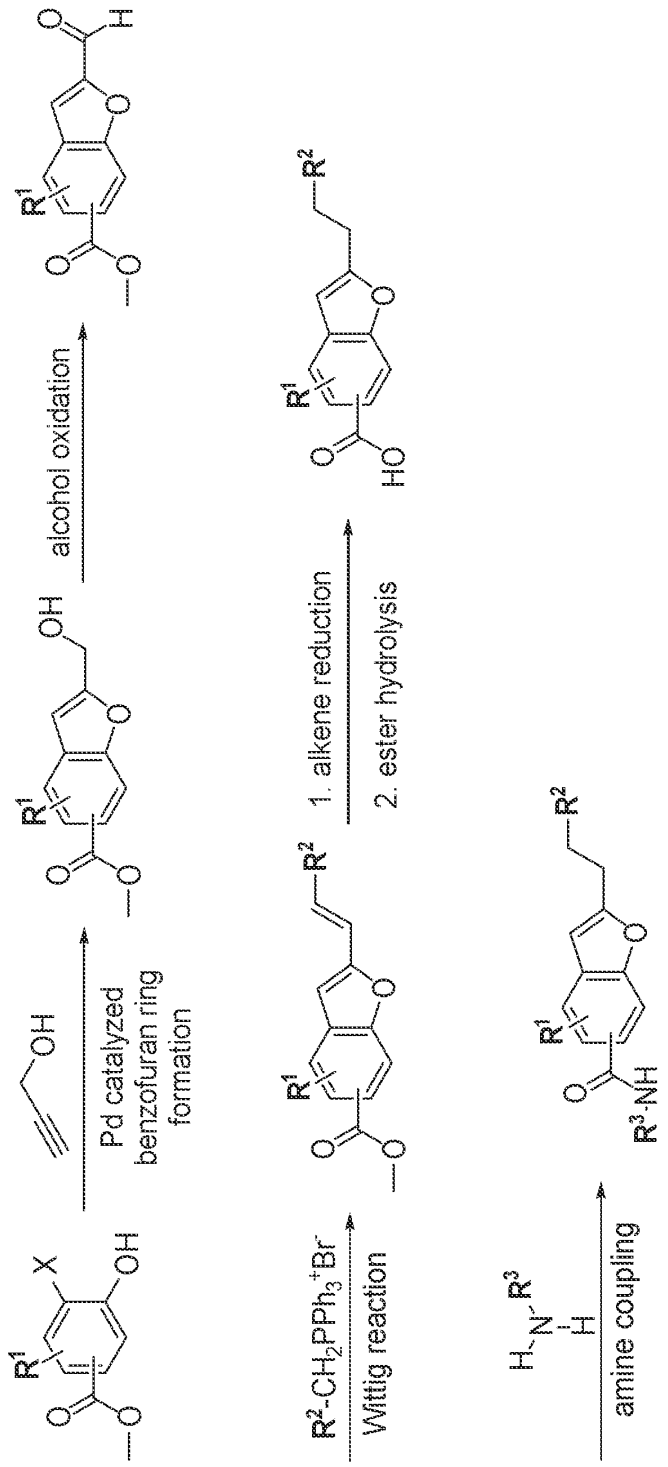

Pd catalyzed benzofuran ring formation
alcohol oxidation
1. alkene reduction
2. ester hydrolysis
Wittig reaction
amine coupling

FIG. 1M

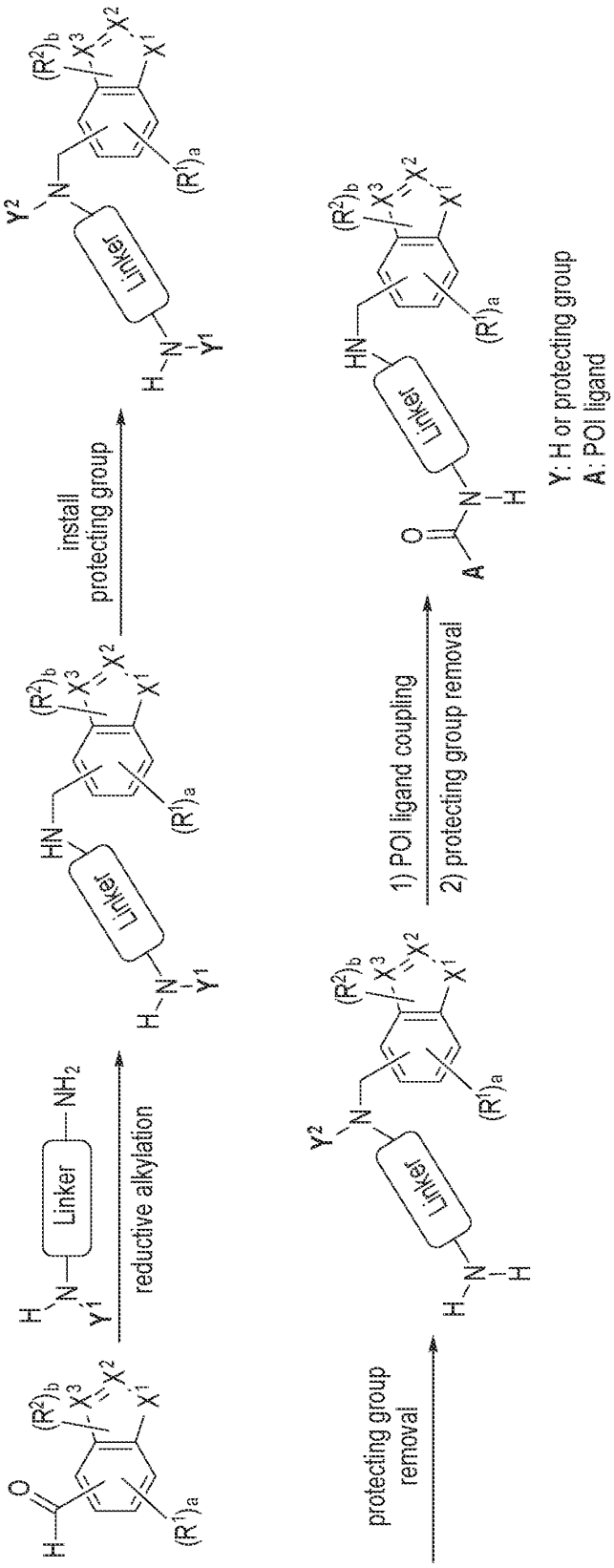

reductive alkylation
install protecting group
1) POI ligand coupling
2) protecting group removal
protecting group removal
Linker
Y: H or protecting group
A: POI ligand

FIG. 2A

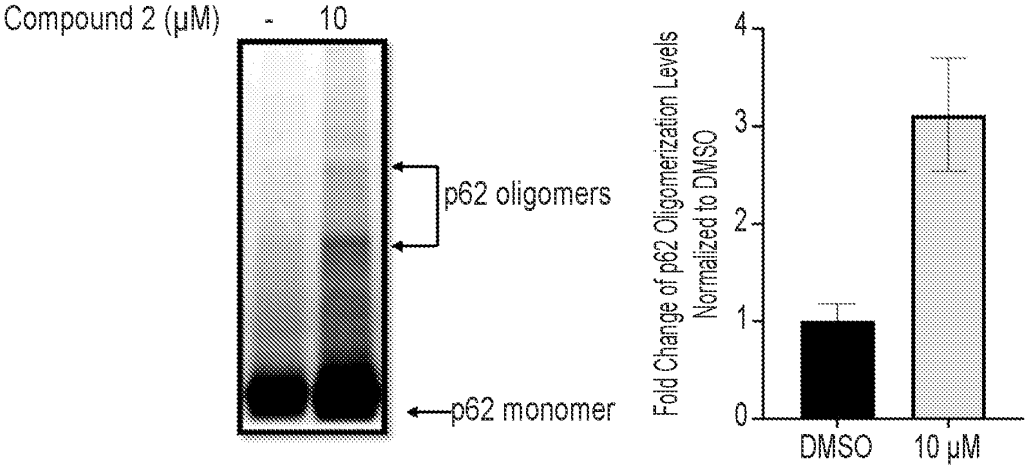


FIG. 2B

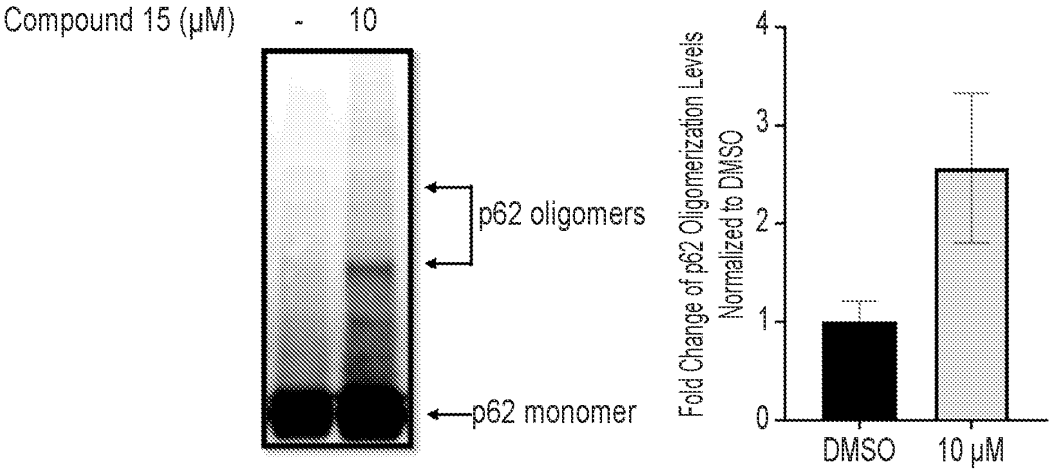


FIG. 2C

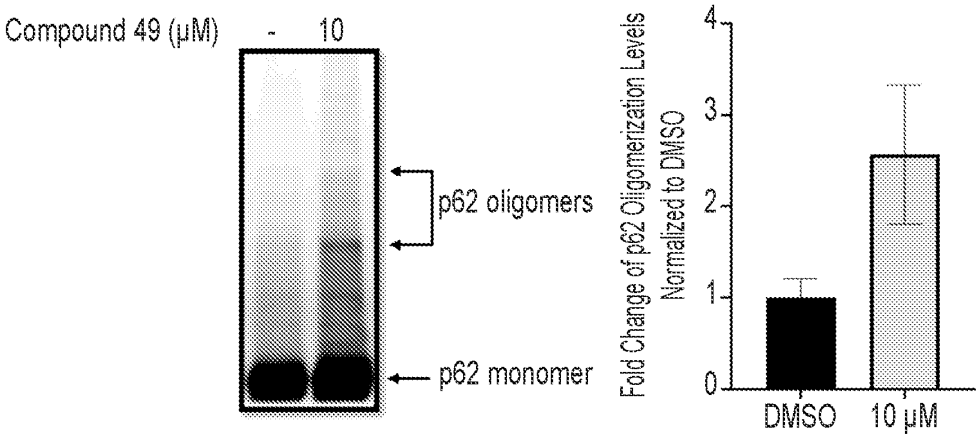


FIG. 3A

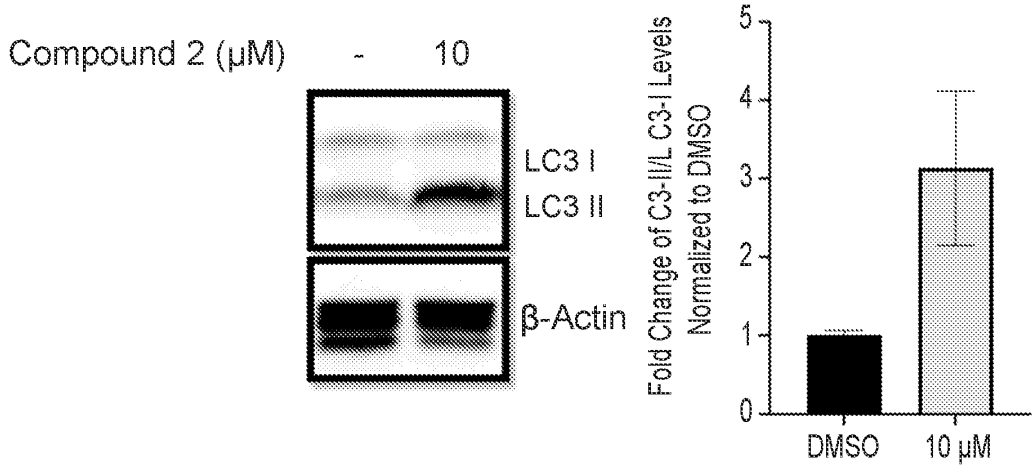


FIG. 3B

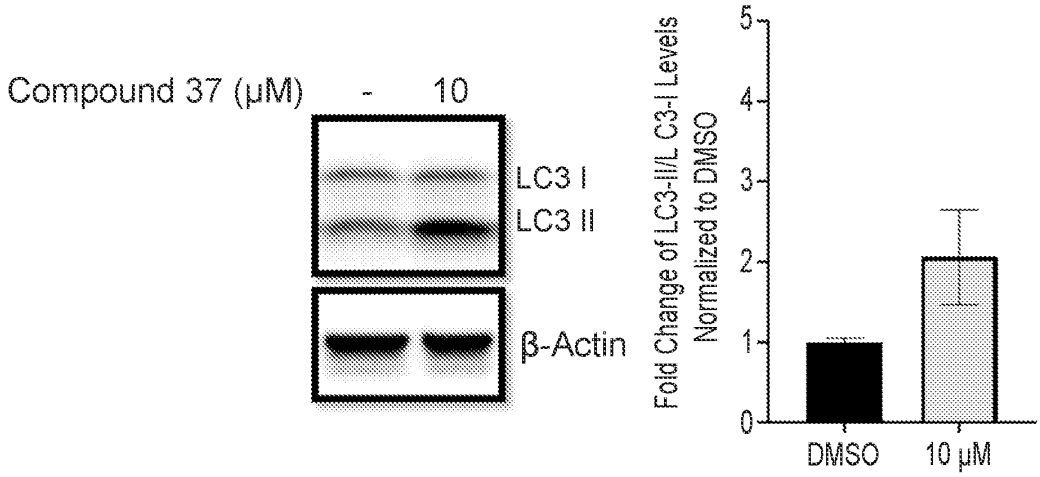
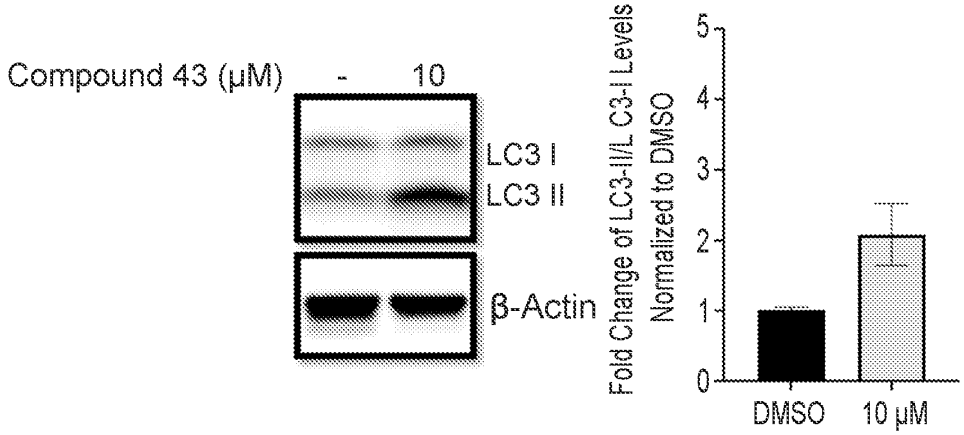


FIG. 3C



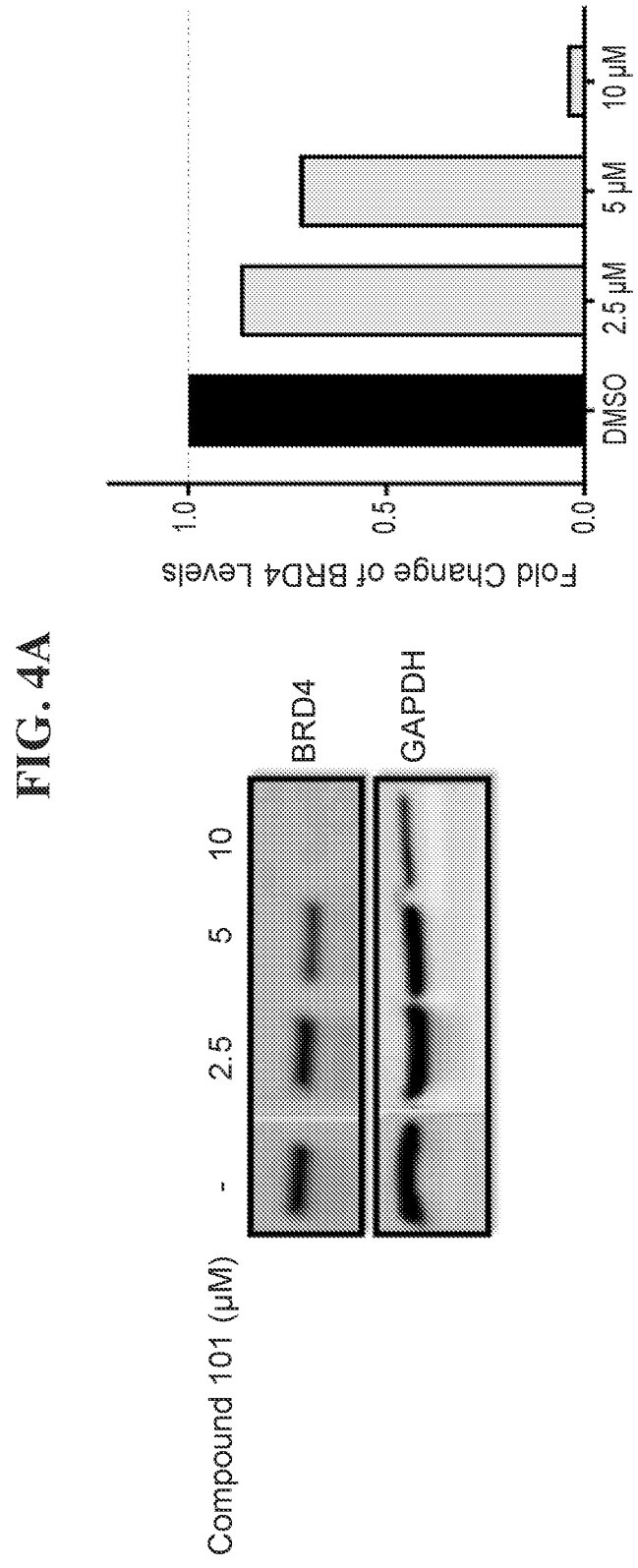
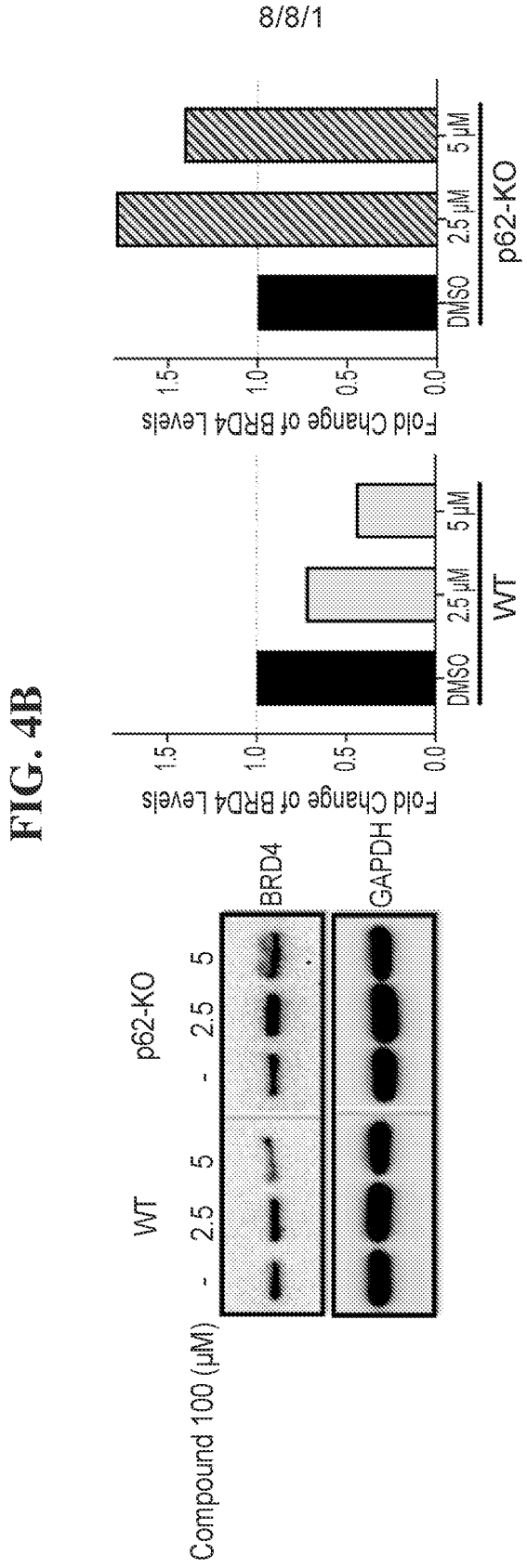

Fold Change of BRD4 Levels
0.0
0.5
1.0
DMSO
2.5 μM
5 μM
10 μM
Compound 101 (μM)
-
2.5
5
10
BRD4
GAPDH

FIG. 4A

8/8/1

FIG. 4B


Compound 100 (μM)
-
2.5
5
WT
-
2.5
5
p62-KO
BRD4
GAPDH
Fold Change of BRD4 Levels
0.0
0.5
1.0
1.5
DMSO
2.5 μM
5 μM
WT
Fold Change of BRD4 Levels
0.0
0.5
1.0
1.5
DMSO
2.5 μM
5 μM
p62-KO

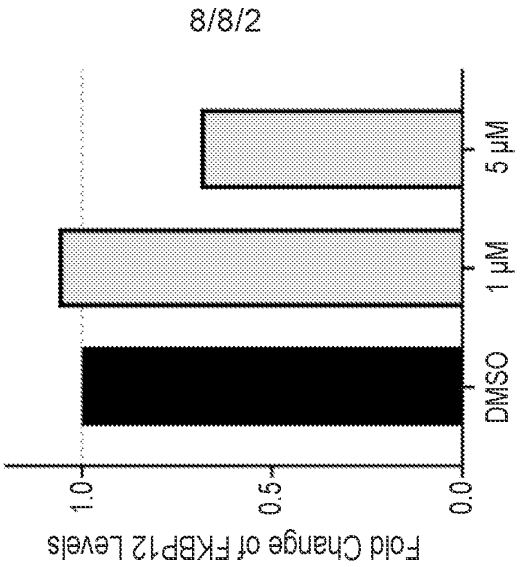
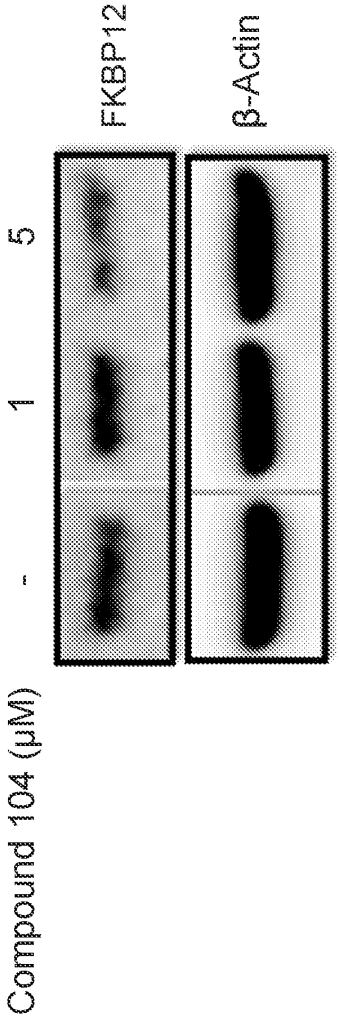

8/8/2
Fold Change of FKBP12 Levels
1.0
0.5
0.0
DMSO
1 μM
5 μM

FIG. 5


FKBP12
β-Actin
Compound 104 (μM)
-
1
5