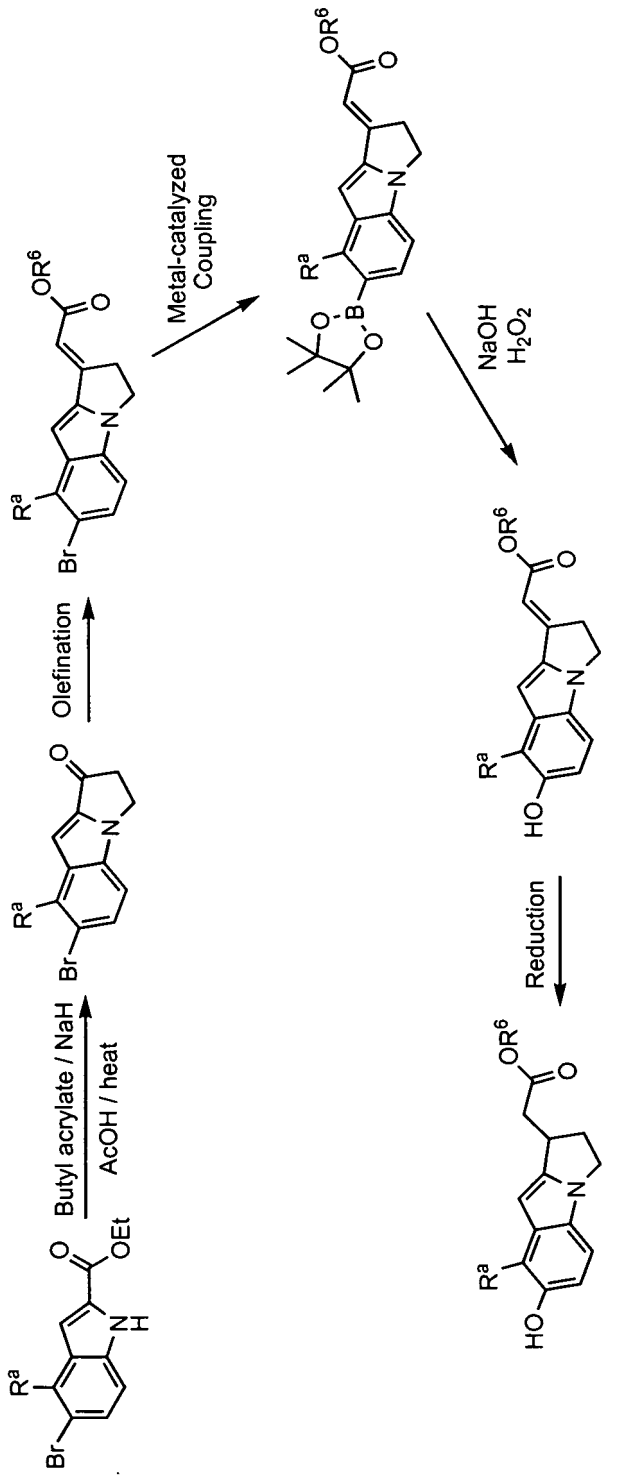

Butyl acrylate / NaH
AcOH / heat
Olefination
Metal-catalyzed Coupling
NaOH
H_2O_2
Reduction
R^a
OR^6
Br
HO
OEt

FIGURE 1

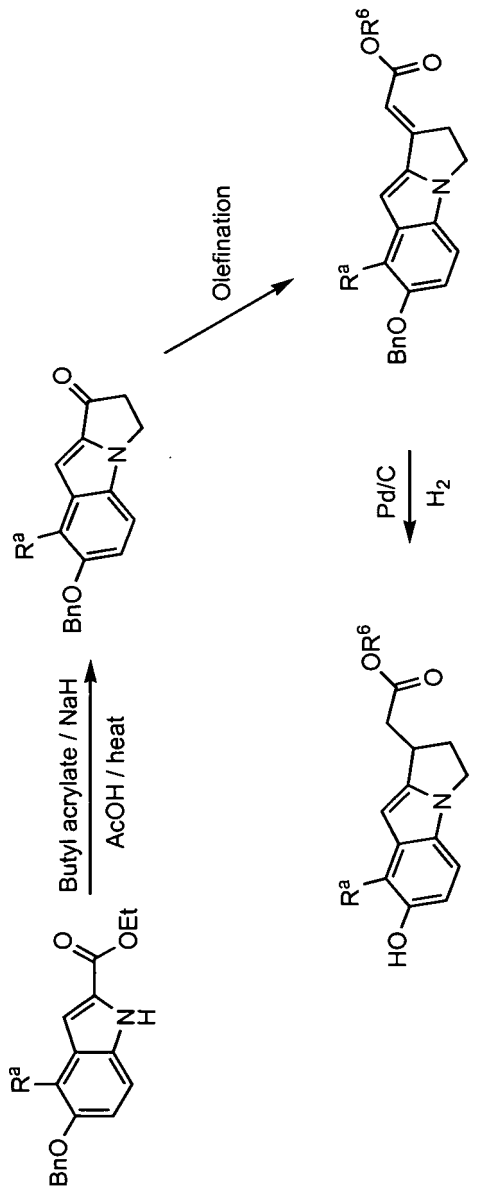

Butyl acrylate / NaH
AcOH / heat
Olefination
Pd/C
H_2
OEt
OR6
BnO
HO
Ra

FIGURE 2

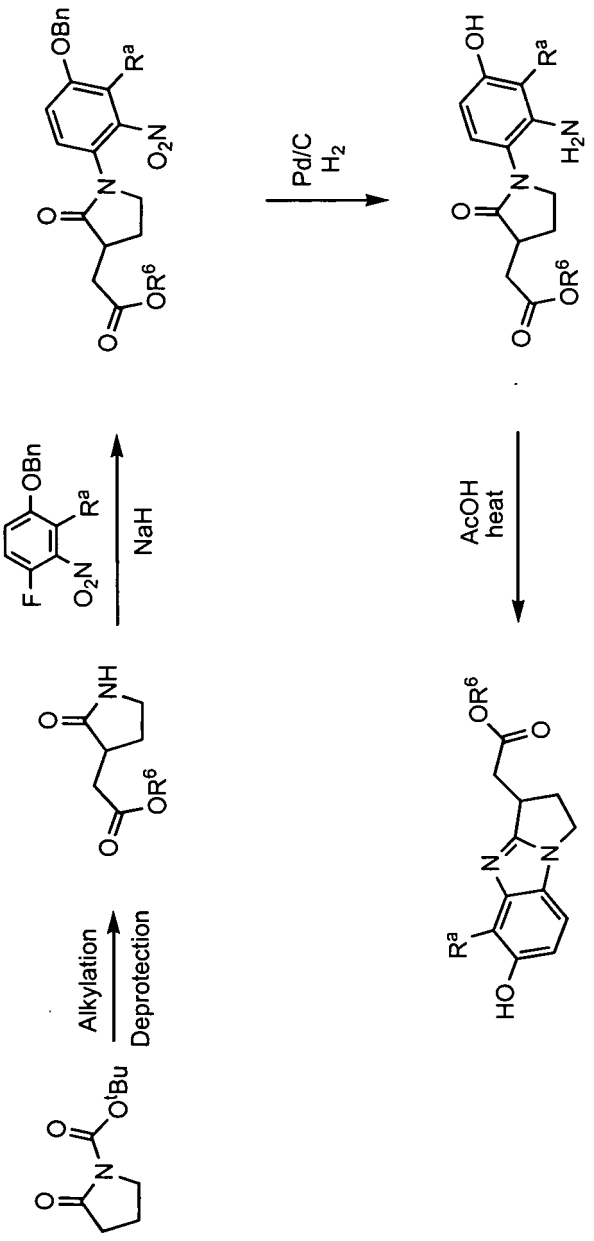

OBn
R^a
O_2N
N
O
OR^6
Pd/C
H_2
OH
H_2N
NaH
F
NH
Alkylation
Deprotection
O^tBu
AcOH
heat
HO

FIGURE 3

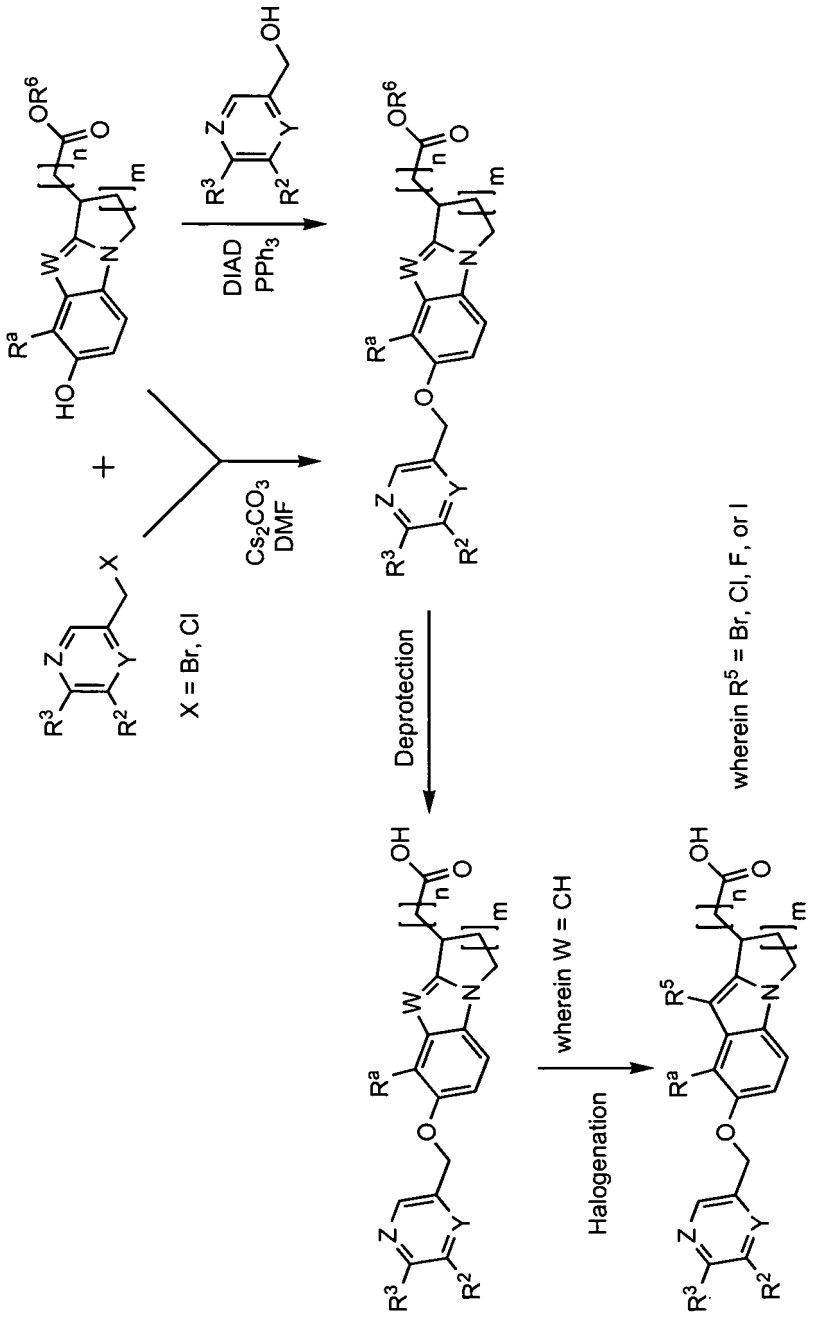

X = Br, Cl
Cs_2CO_3
DMF
DIAD
PPh_3
Deprotection
wherein W = CH
Halogenation
wherein R^5 = Br, Cl, F, or I

FIGURE 4

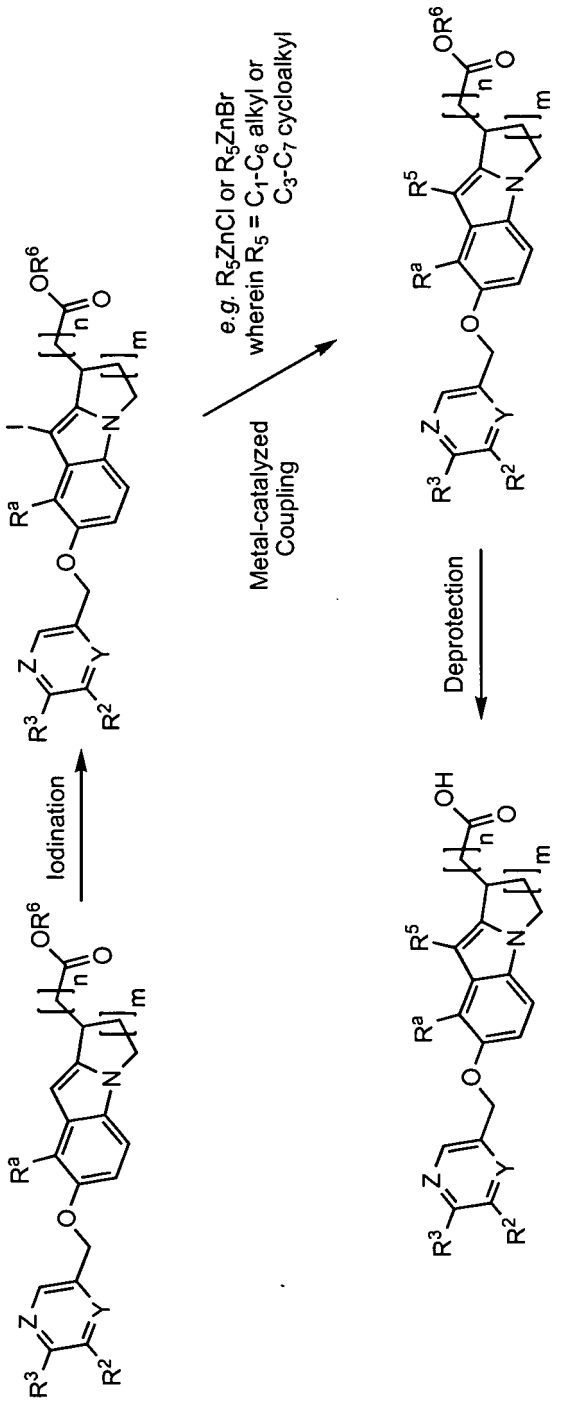

Iodination
e.g. R5ZnCl or R5ZnBr
wherein R5 = C1-C6 alkyl or
C3-C7 cycloalkyl
Metal-catalyzed
Coupling
Deprotection

FIGURE 5

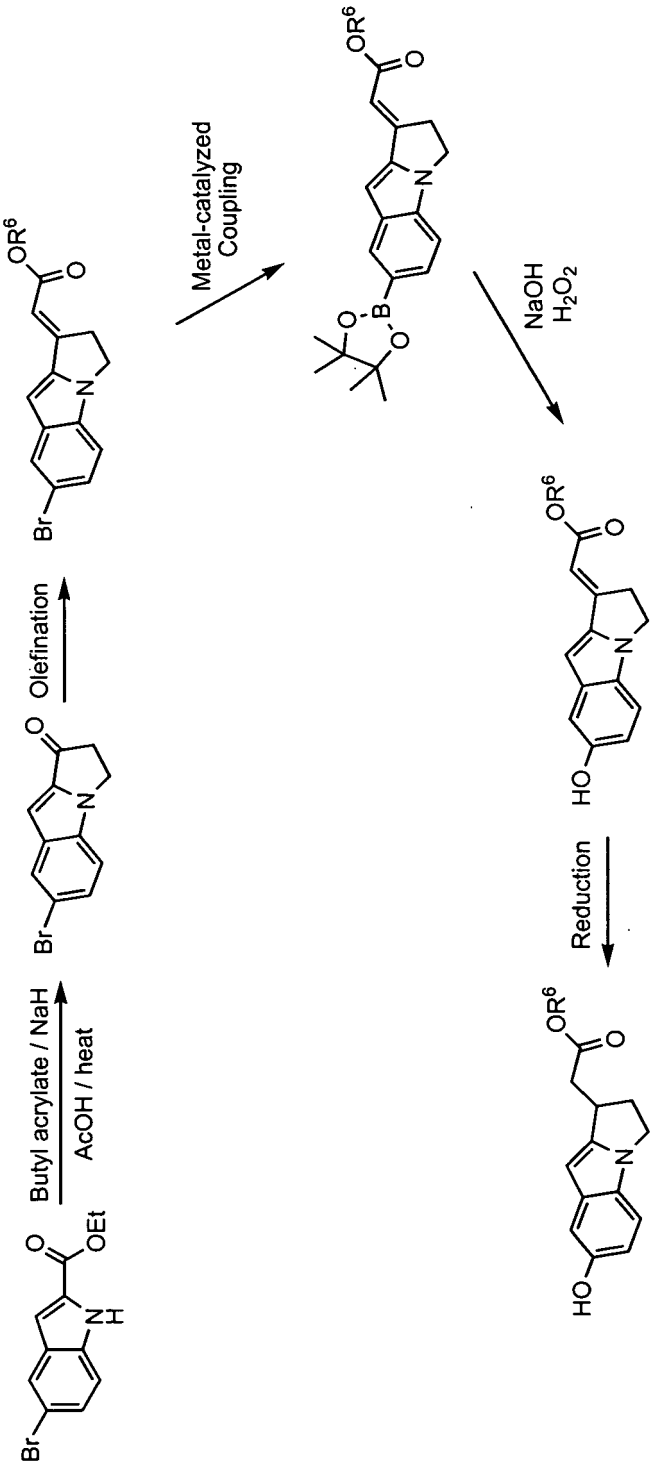

Butyl acrylate / NaH
AcOH / heat
Olefination
Metal-catalyzed Coupling
NaOH
H_2O_2
Reduction
OEt
Br
OR6
HO

FIGURE 6

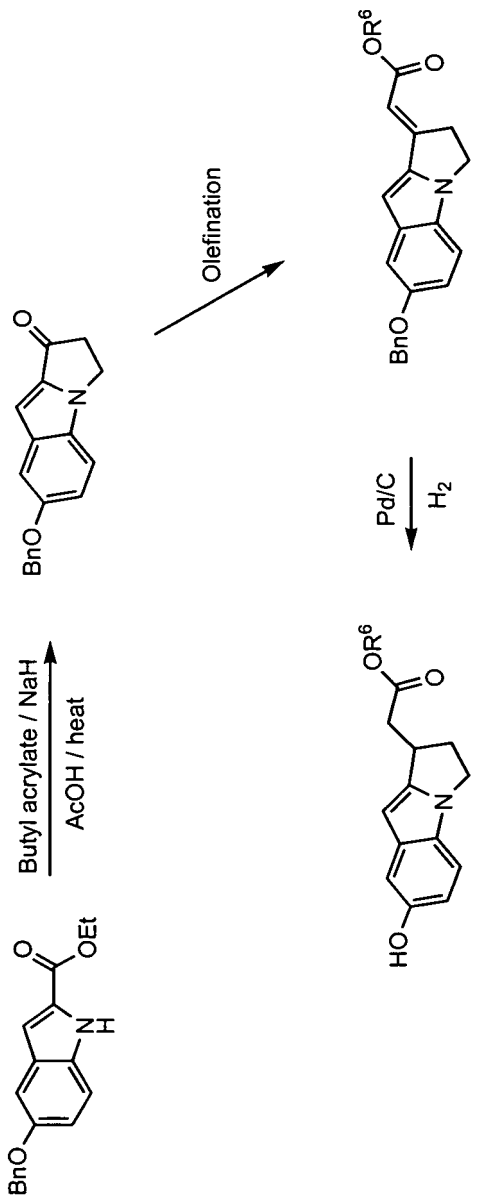

Butyl acrylate / NaH
AcOH / heat
Olefination
Pd/C
H_2
BnO
HO
OEt
OR^6
O
N
H

FIGURE 7

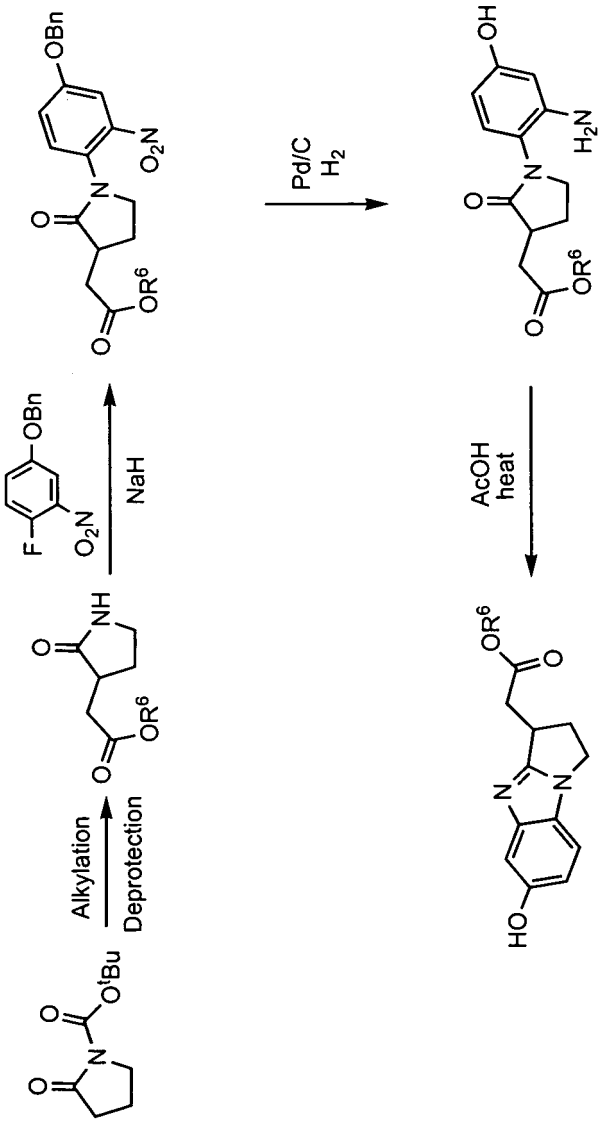

OBn
O2N
N
O
OR6
O
Pd/C
H2
OH
H2N
NaH
F
NH
Alkylation
Deprotection
AcOH
heat
OtBu
HO

FIGURE 8

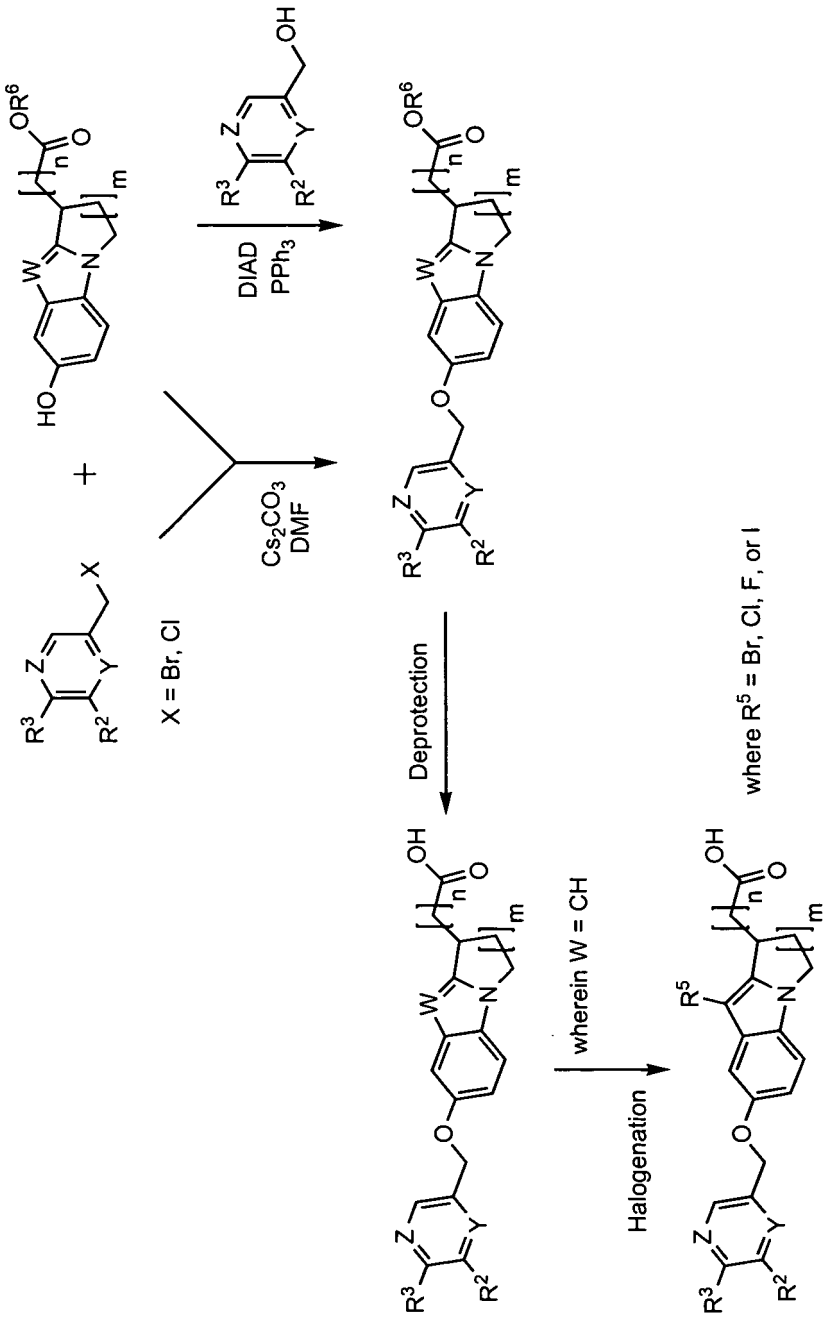

X = Br, Cl
Cs_2CO_3
DMF
DIAD
PPh_3
Deprotection
wherein W = CH
Halogenation
where R^5 = Br, Cl, F, or I

FIGURE 9

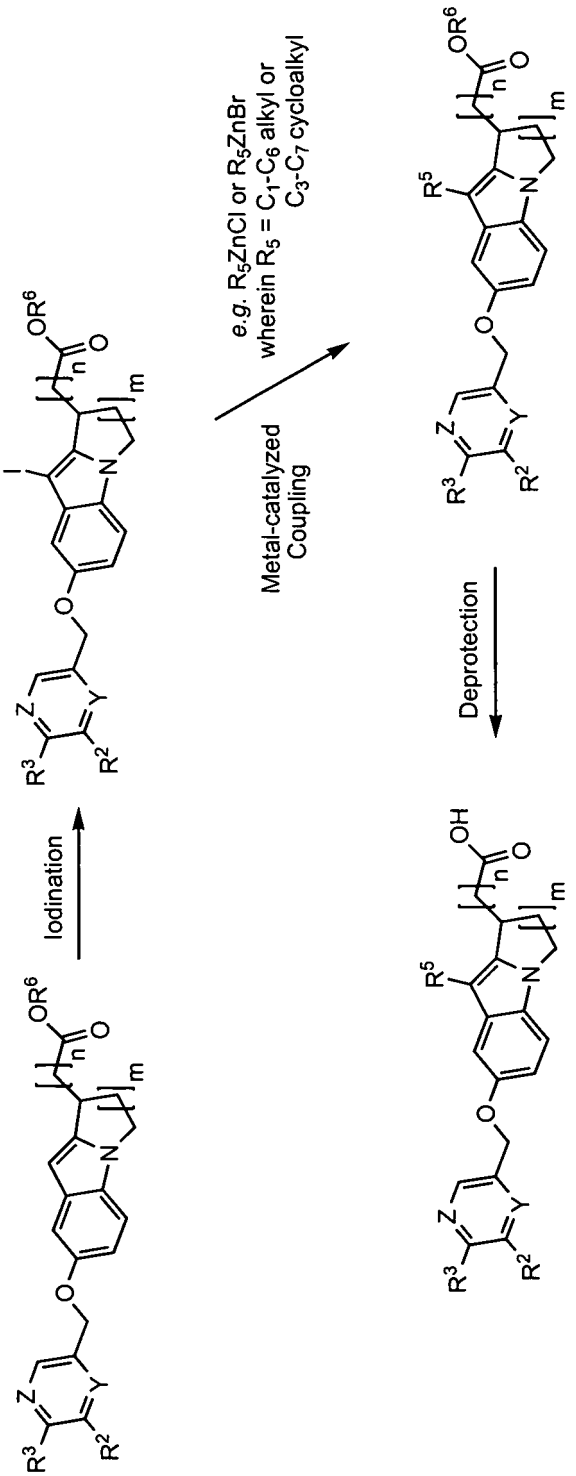

Iodination
e.g. R5ZnCl or R5ZnBr
wherein R5 = C1-C6 alkyl or
C3-C7 cycloalkyl
Metal-catalyzed
Coupling
Deprotection

FIGURE 10

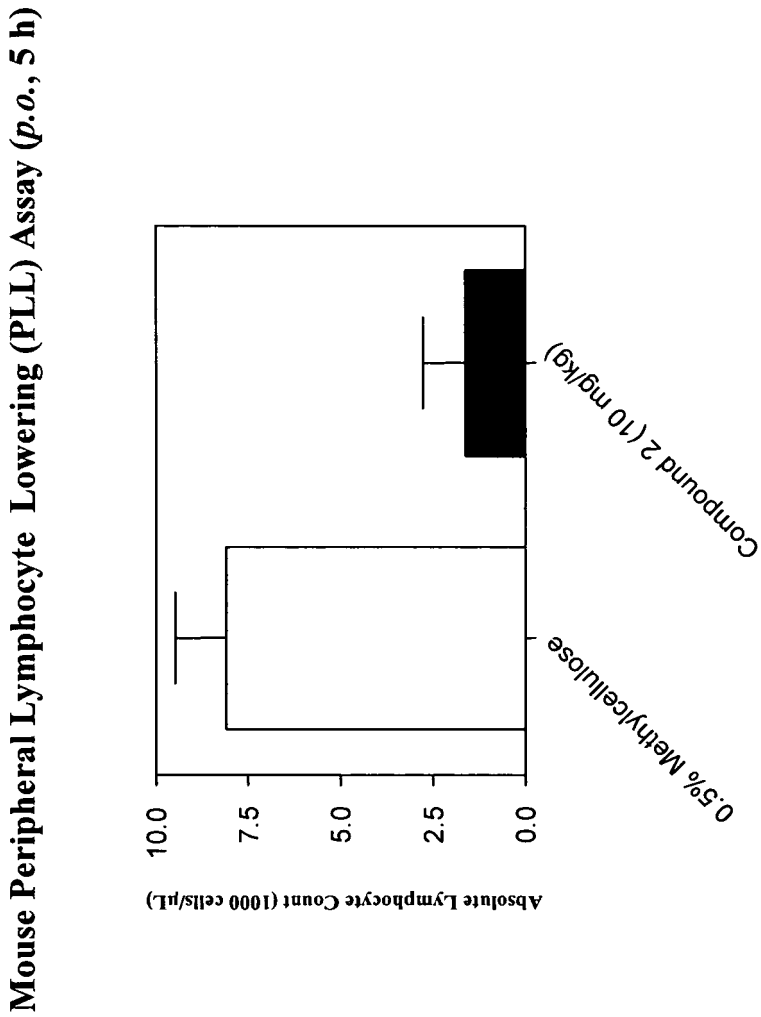

Mouse Peripheral Lymphocyte Lowering (PLL) Assay (p.o., 5 h)
Absolute Lymphocyte Count (1000 cells/μL)
10.0
7.5
5.0
2.5
0.0
0.5% Methylcellulose
Compound 2 (10 mg/kg)

FIGURE 11

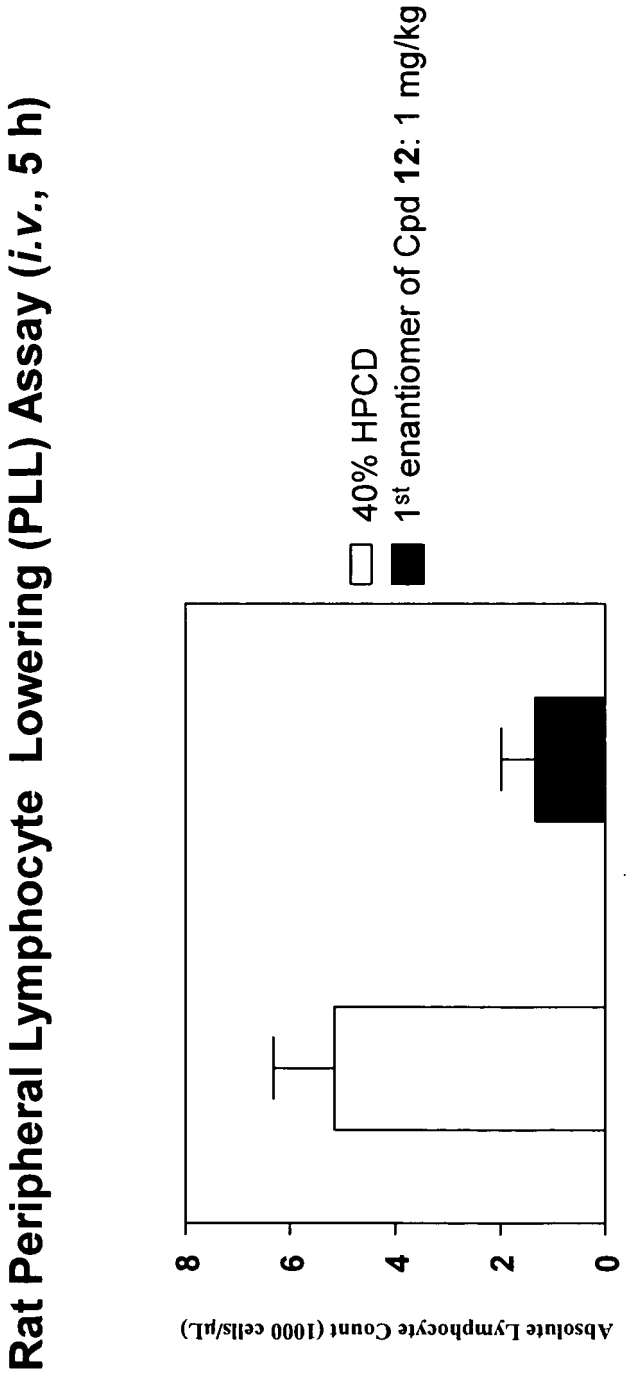

Rat Peripheral Lymphocyte Lowering (PLL) Assay (i.v., 5 h)
40% HPCD
1st enantiomer of Cpd 12: 1 mg/kg
Absolute Lymphocyte Count (1000 cells/μL)
0
2
4
6
8

FIGURE 12


Rat Peripheral Lymphocyte Lowering (PLL) Assay (i.v., 5 h)
40% HPCD
2nd enantiomer of Cpd 12: 1 mg/kg
Absolute Lymphocyte Count (1000 cells/μL)
0
2
4
6
8

FIGURE 13

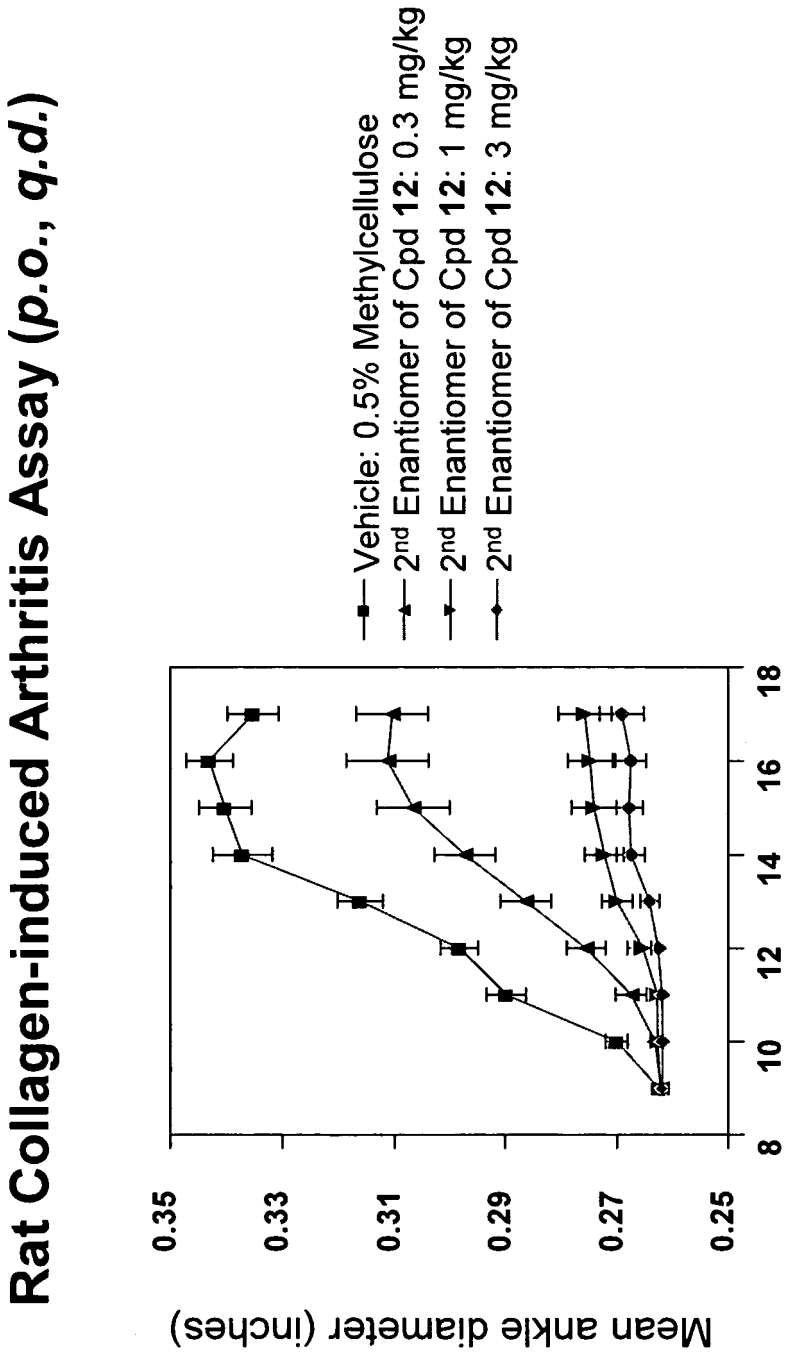

Rat Collagen-induced Arthritis Assay (p.o., q.d.)
Vehicle: 0.5% Methylcellulose
2nd Enantiomer of Cpd 12: 0.3 mg/kg
2nd Enantiomer of Cpd 12: 1 mg/kg
2nd Enantiomer of Cpd 12: 3 mg/kg
Mean ankle diameter (inches)
0.35
0.33
0.31
0.29
0.27
0.25
8
10
12
14
16
18
Days

FIGURE 14