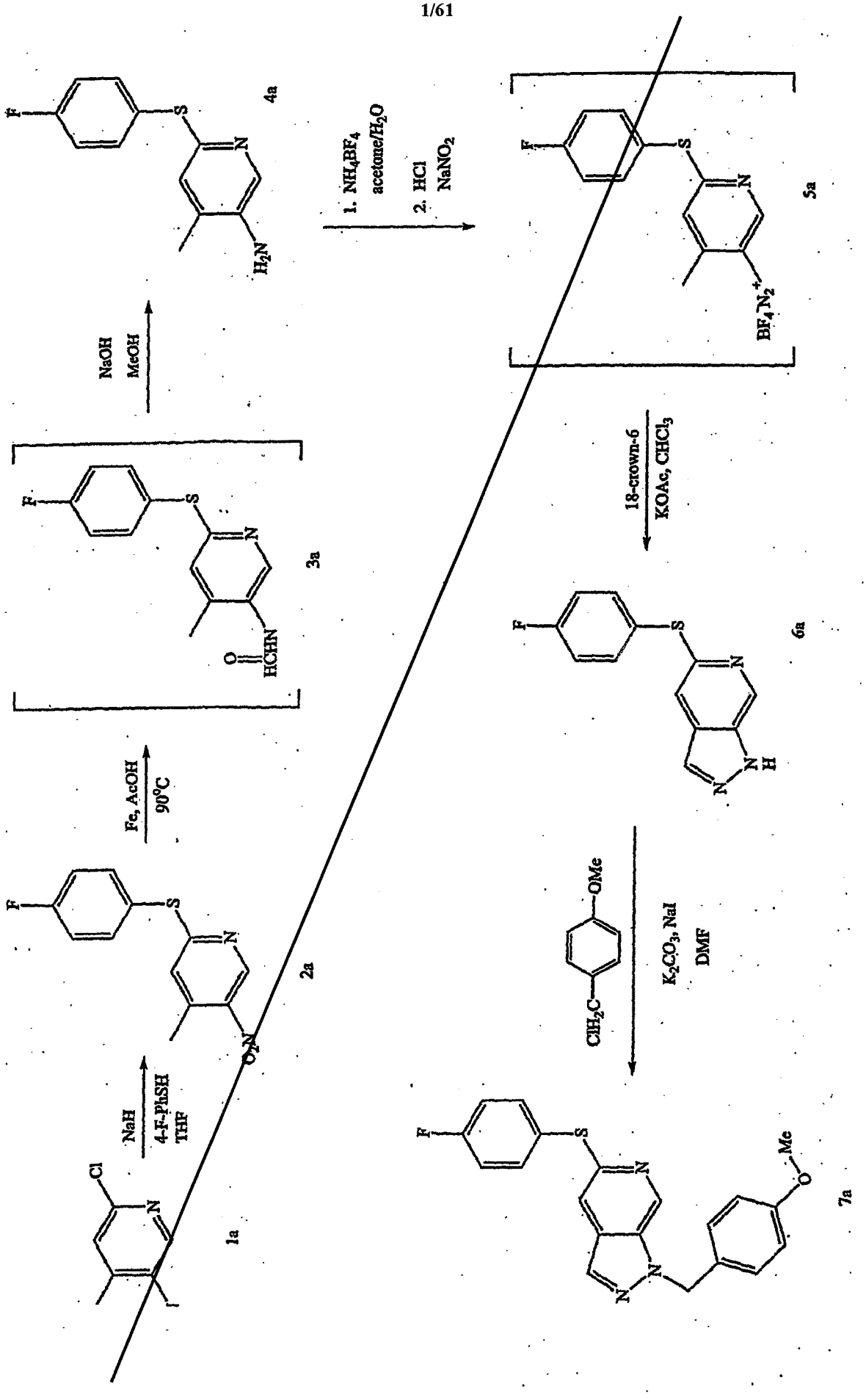

NaH
4-F-PhSH
THF
Fe, AcOH
90°C
NaOH
MeOH
1. NH_4BF_4
acetone/H_2O
2. HCl
$NaNO_2$
18-crown-6
KOAc, $CHCl_3$
K_2CO_3, NaI
DMF
1a
2a
3a
4a
5a
6a
7a

FIG. 1

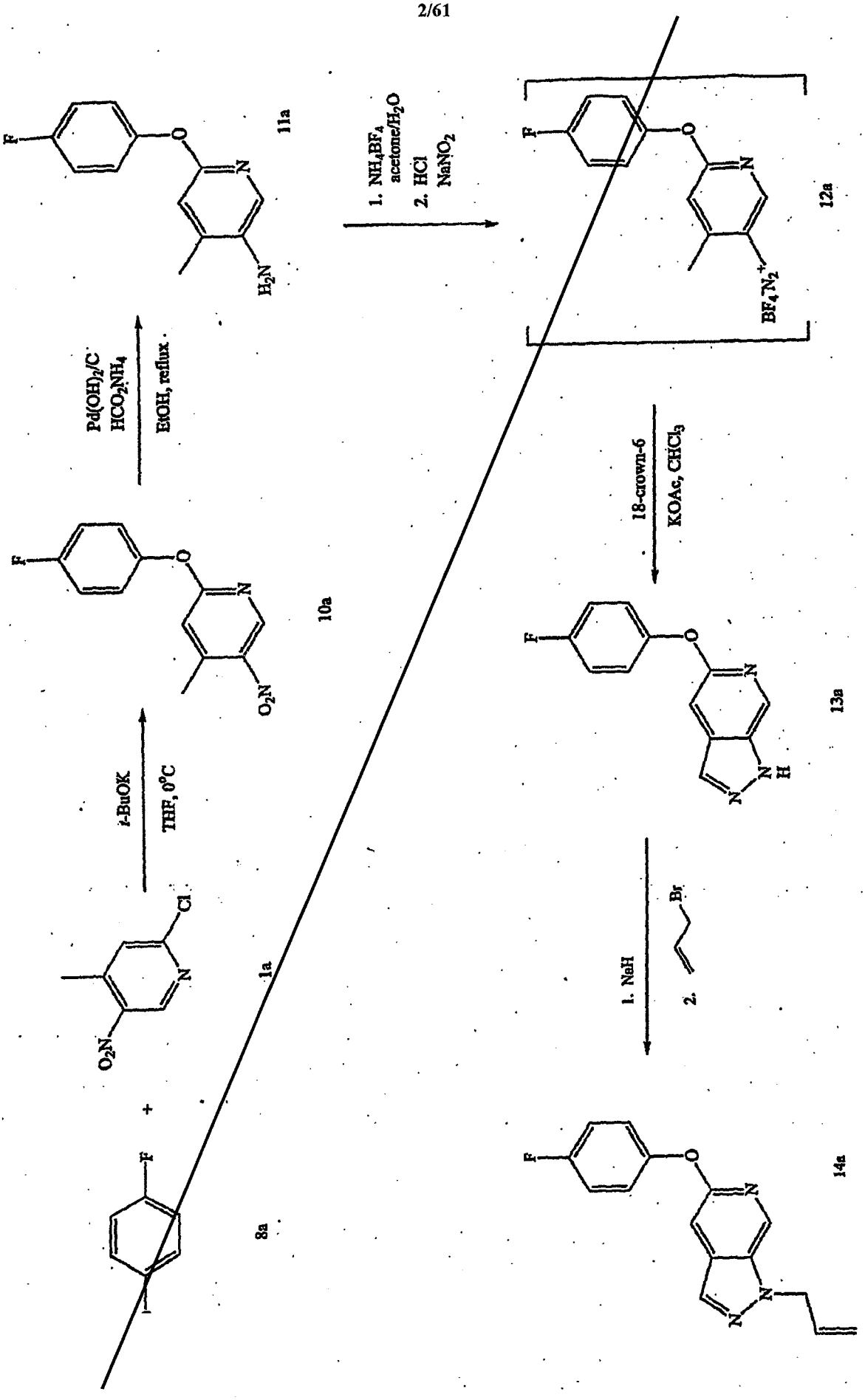

F
O
N
H_2N
11a
$Pd(OH)_2/C$
HCO_2NH_4
EtOH, reflux
O_2N
10a
t-BuOK
THF, 0°C
Cl
O_2N
1a
+
F
I
8a
1. NH_4BF_4
acetone/H_2O
2. HCl
$NaNO_2$
$BF_4N_2^+$
12a
18-crown-6
KOAc, $CHCl_3$
H
13a
1. NaH
2.
Br
14a

FIG. 2

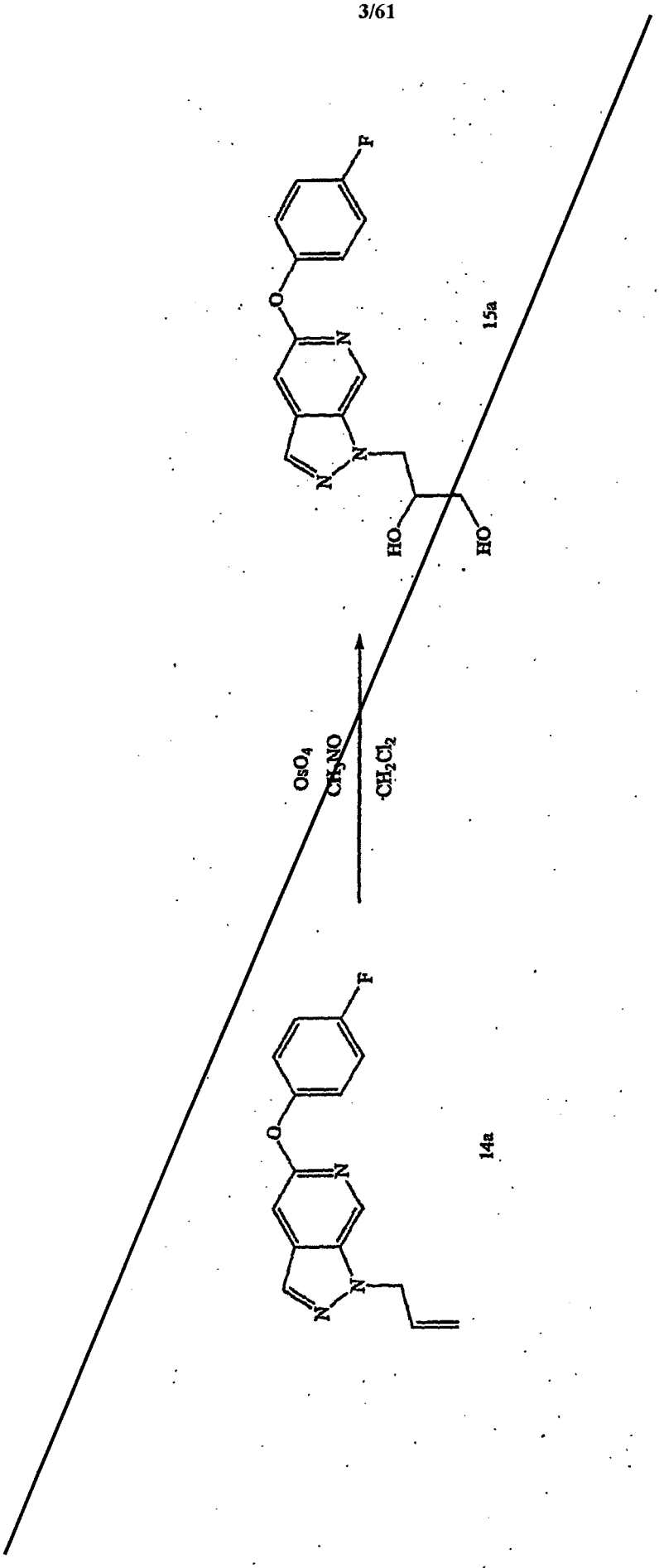


FIG. 3

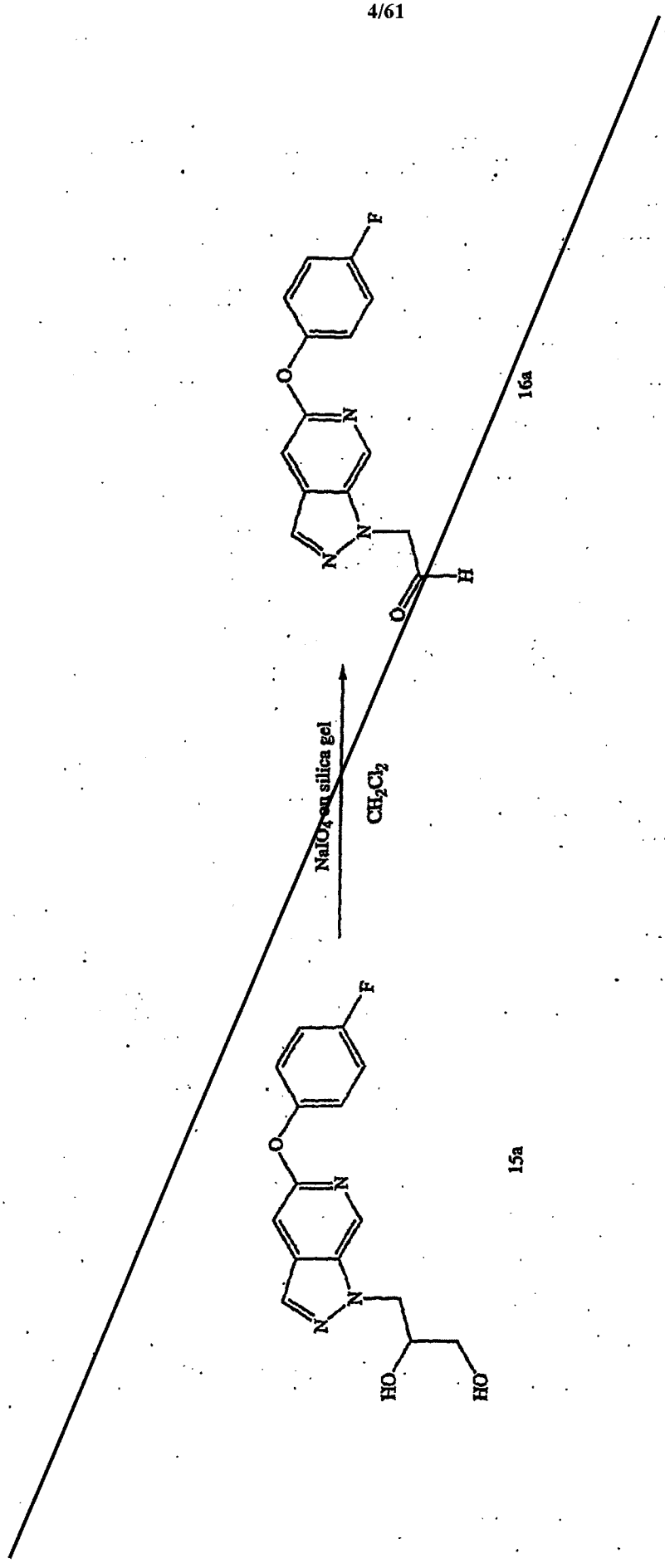


FIG. 4

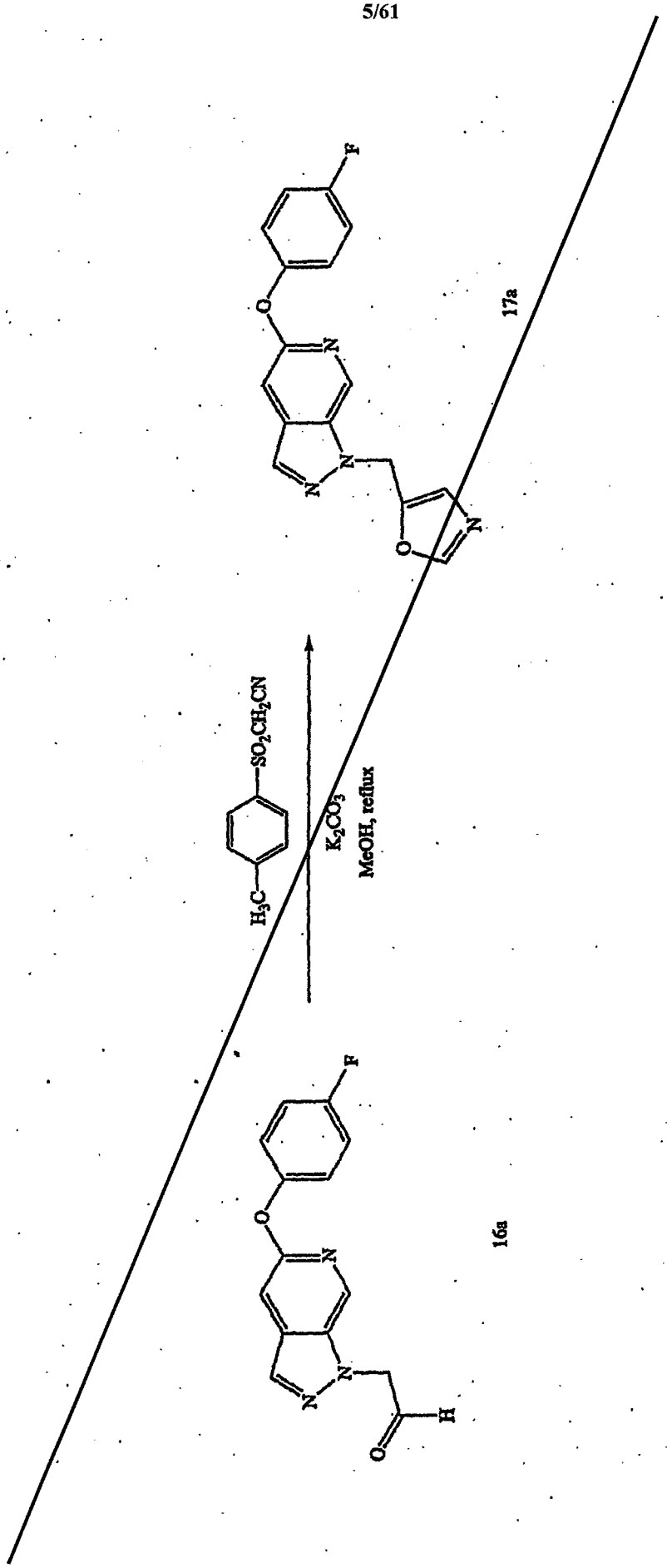


FIG. 5

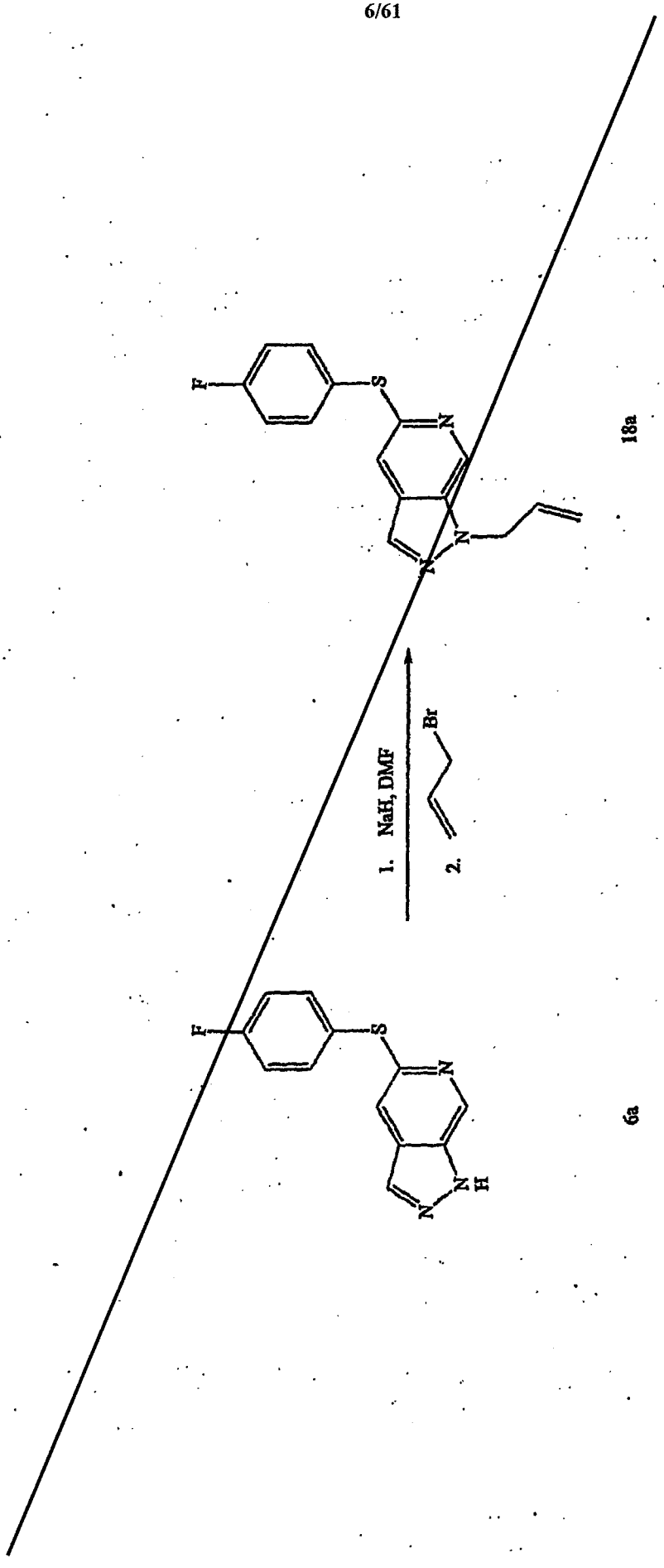


FIG. 6

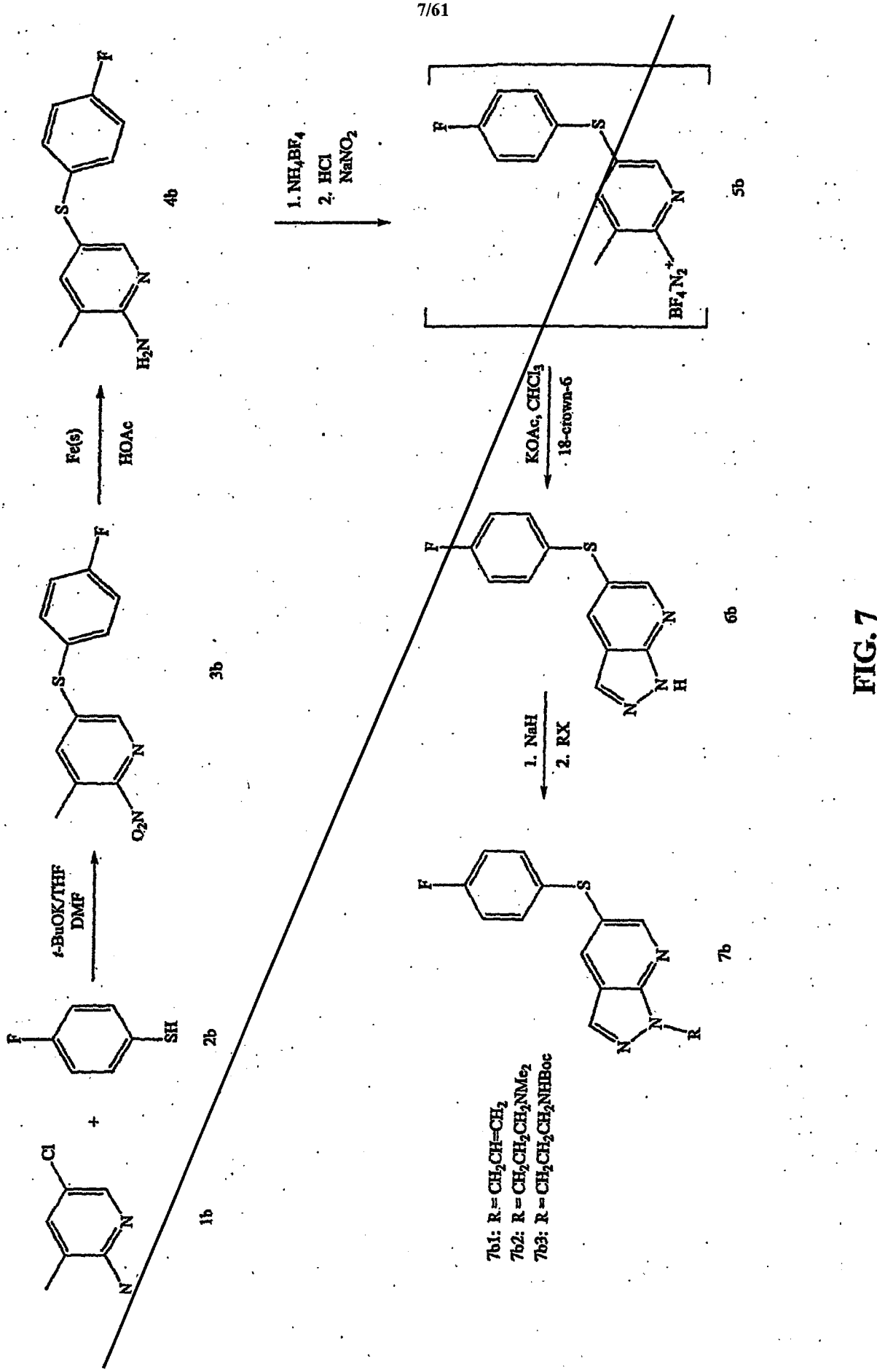

t-BuOK/THF
DMF
Fe(s)
HOAc
1. NH4BF4
2. HCl
NaNO2
KOAc, CHCl3
18-crown-6
1. NaH
2. RX
1b
2b
3b
4b
5b
6b
7b
7b1: R = CH2CH=CH2
7b2: R = CH2CH2CH2NMe2
7b3: R = CH2CH2CH2NHBoc

FIG. 7

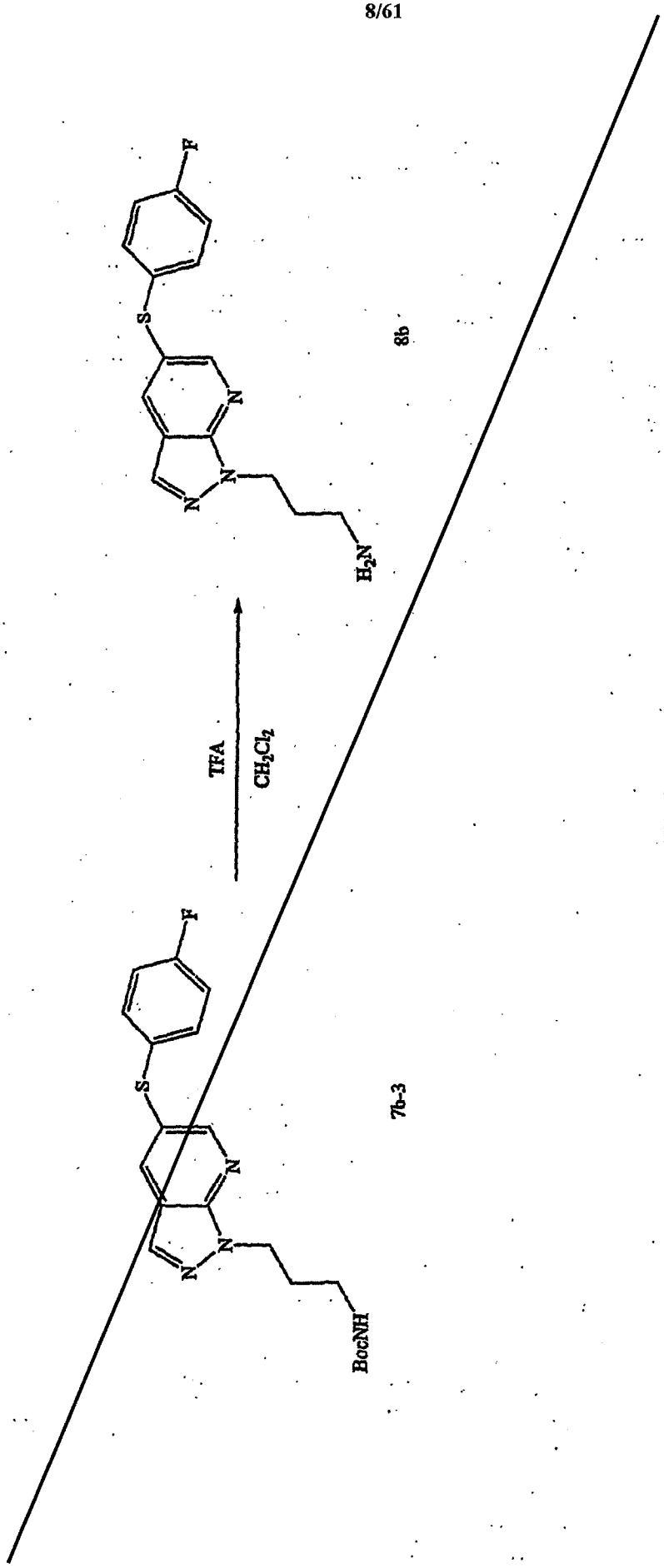


FIG. 8

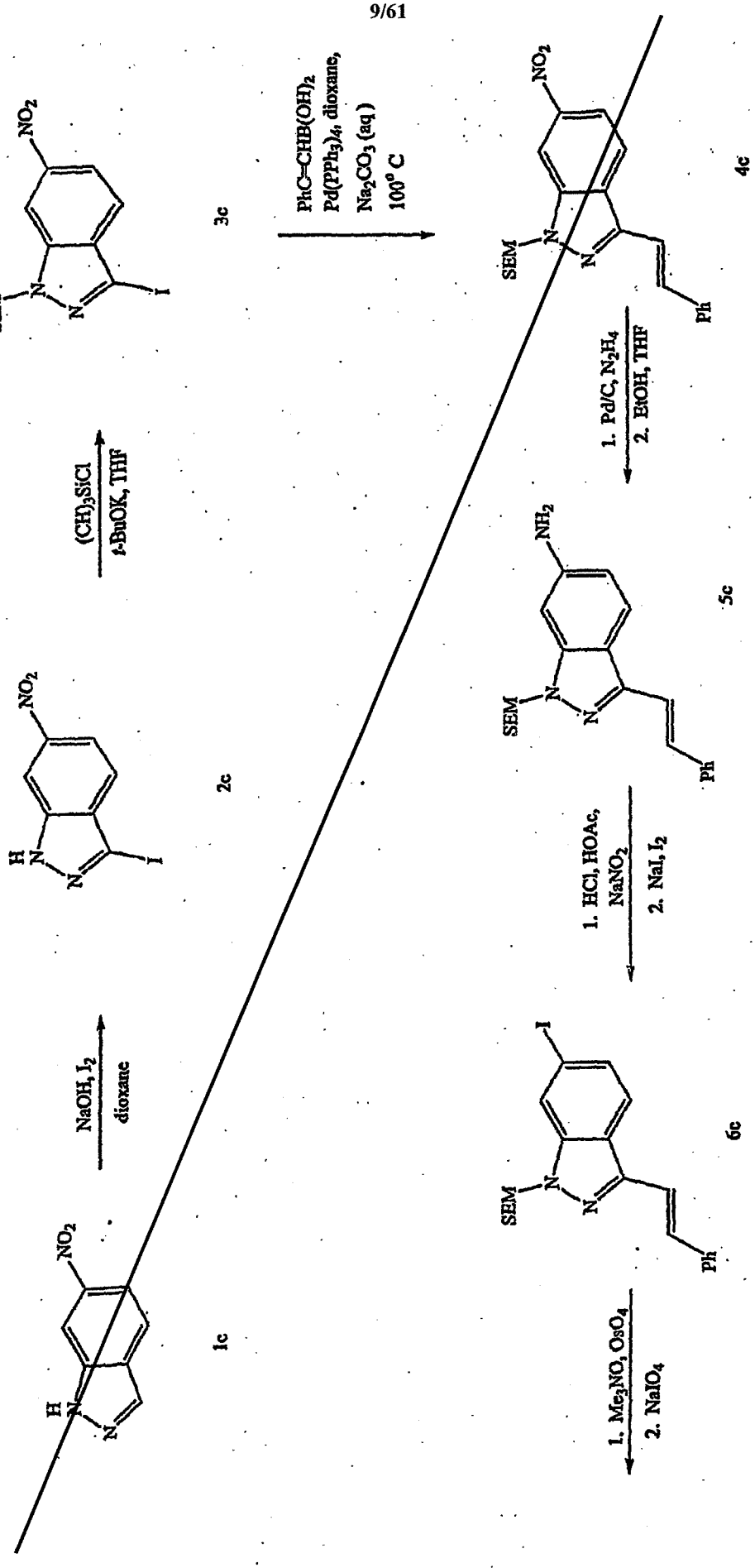

NaOH, I2
dioxane
(CH3)3SiCl
t-BuOK, THF
PhC=CHB(OH)2
Pd(PPh3)4, dioxane,
Na2CO3 (aq)
100° C
1. Pd/C, N2H4
2. EtOH, THF
1. HCl, HOAc,
NaNO2
2. NaI, I2
1. Me3NO, OsO4
2. NaIO4
1c
2c
3c
4c
5c
6c
SEM
Ph

FIG. 9A

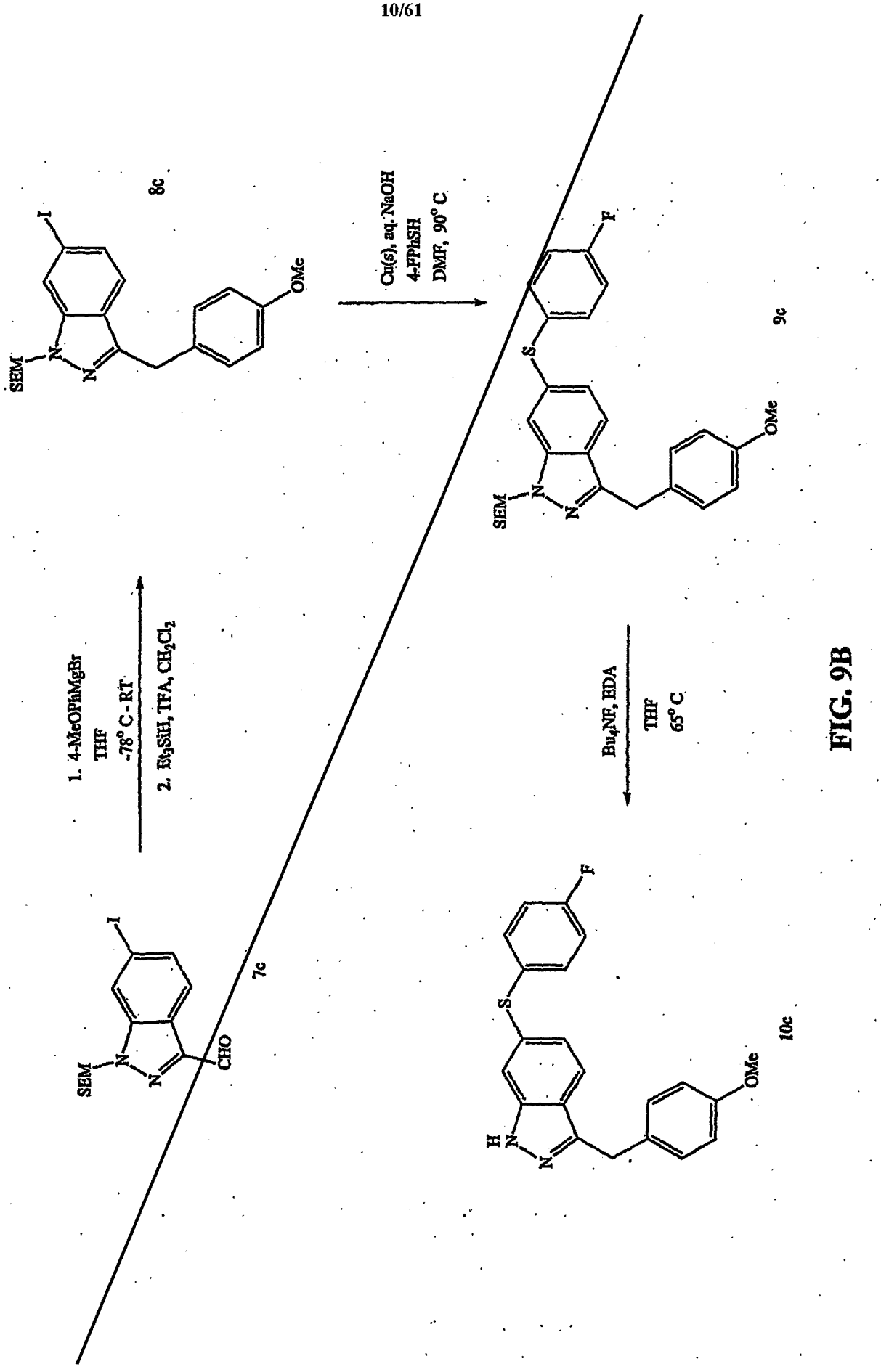

8c
Cu(s), aq. NaOH
4-FPhSH
DMF, 90° C
9c
1. 4-MeOPhMgBr
THF
-78° C - RT
2. Et3SiH, TFA, CH2Cl2
7c
Bu4NF, EDA
THF
65° C
10c

FIG. 9B

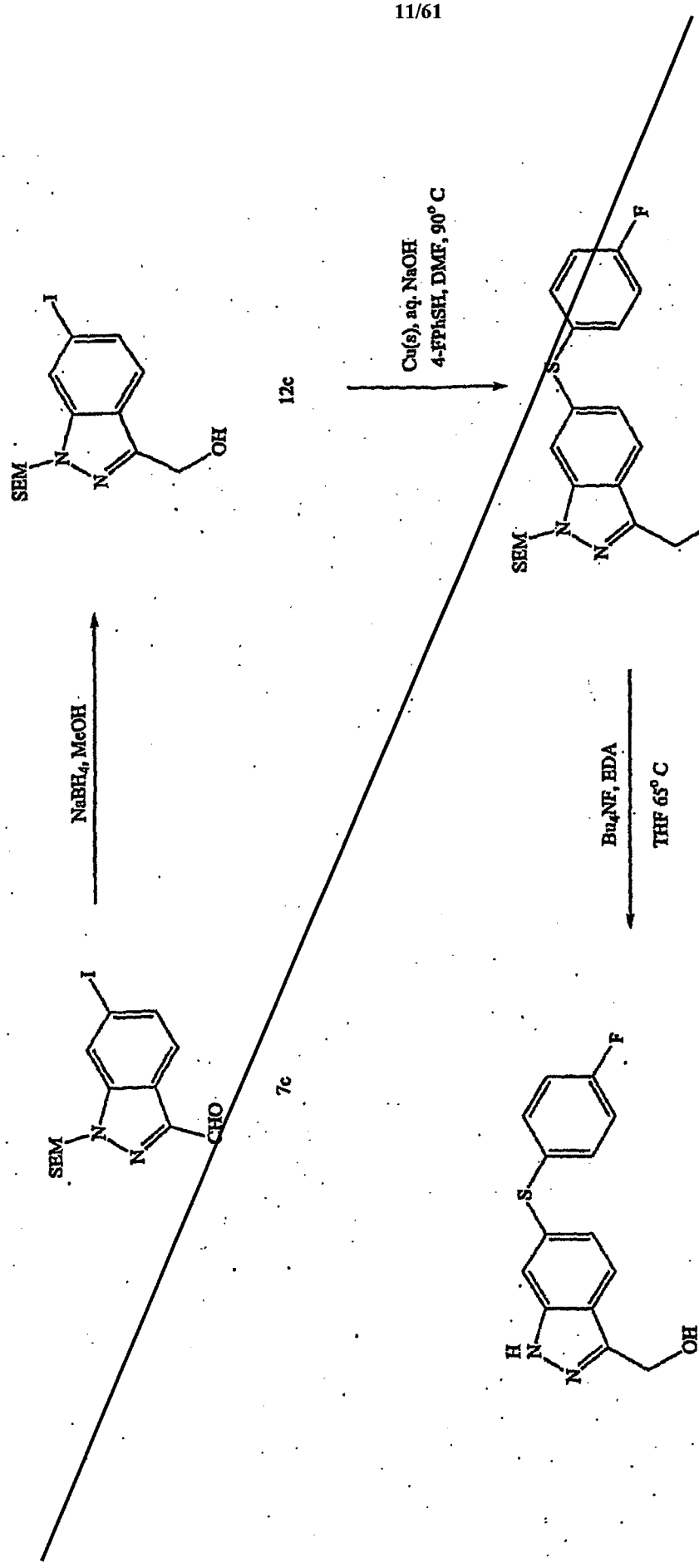

NaBH4, MeOH
Cu(s), aq. NaOH
4-FPhSH, DMF, 90° C
Bu4NF, EDA
THF 65° C
SEM
OH
CHO
F
S
I
12c
13c
7c
14c

FIG. 10

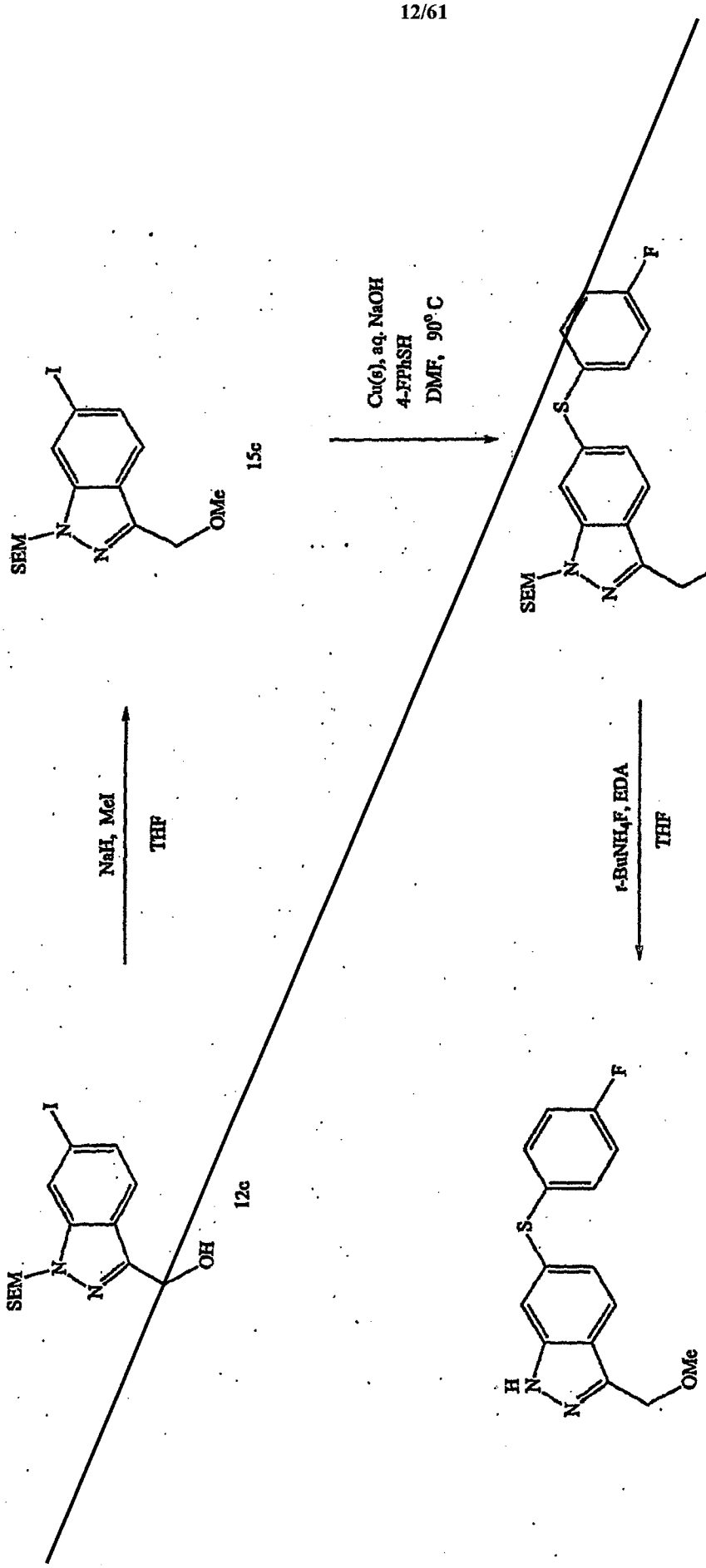

SEM
I
OMe
15c
Cu(0), aq. NaOH
4-FPhSH
DMF, 90° C
F
S
16c
NaH, MeI
THF
t-BuNH4F, EDA
THF
OH
12c
17c
H

FIG. 11

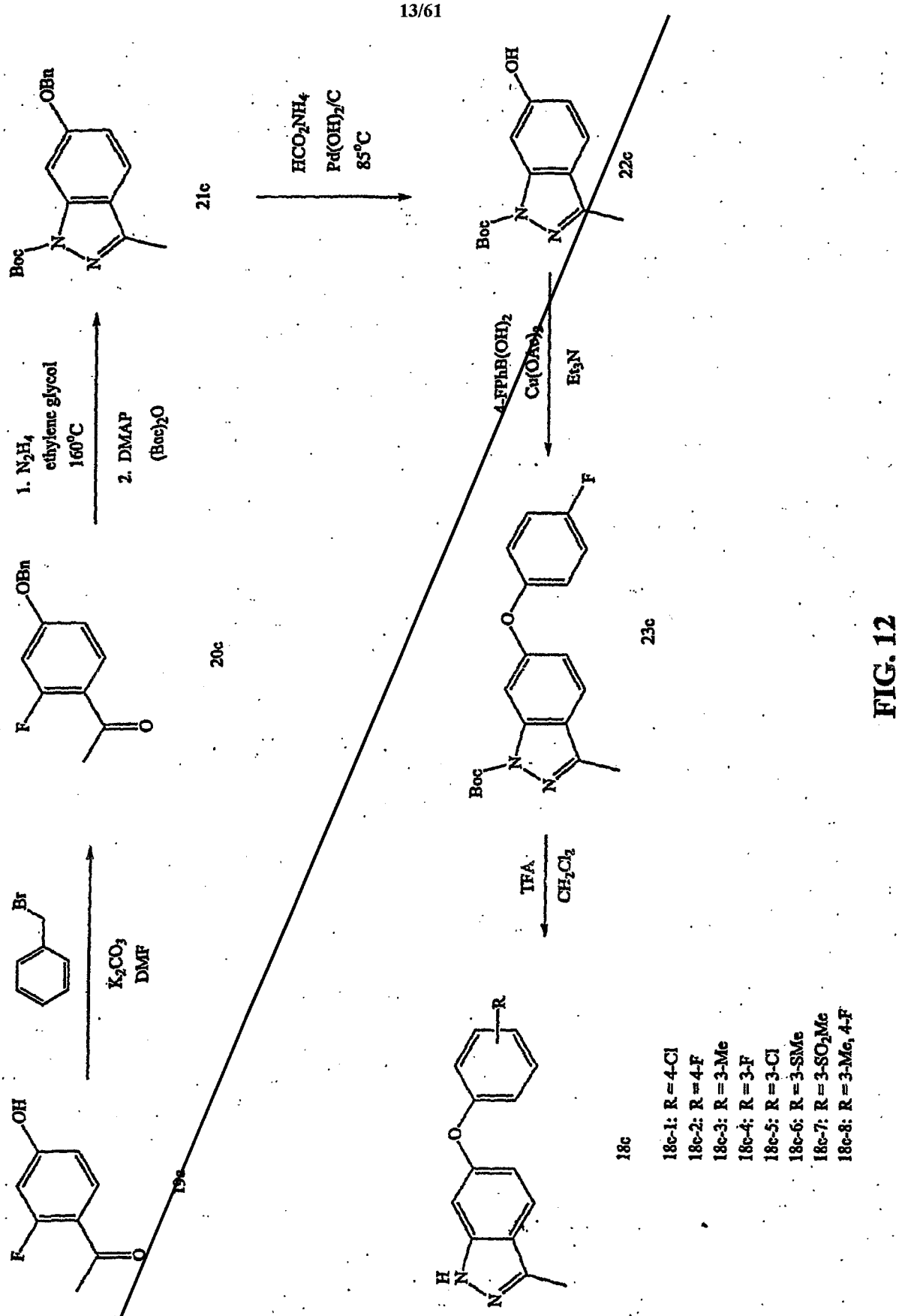

OBn
Boc
21c
1. N_2H_4 ethylene glycol 160°C
2. DMAP $(Boc)_2O$
HCO_2NH_4 $Pd(OH)_2/C$ 85°C
OH
22c
4-FPhB(OH)$_2$ $Cu(OAc)_2$ Et_3N
F
20c
23c
Br
K_2CO_3 DMF
TFA CH_2Cl_2
19c
18c
18c-1: R = 4-Cl
18c-2: R = 4-F
18c-3: R = 3-Me
18c-4: R = 3-F
18c-5: R = 3-Cl
18c-6: R = 3-SMe
18c-7: R = 3-SO_2Me
18c-8: R = 3-Me, 4-F

FIG. 12

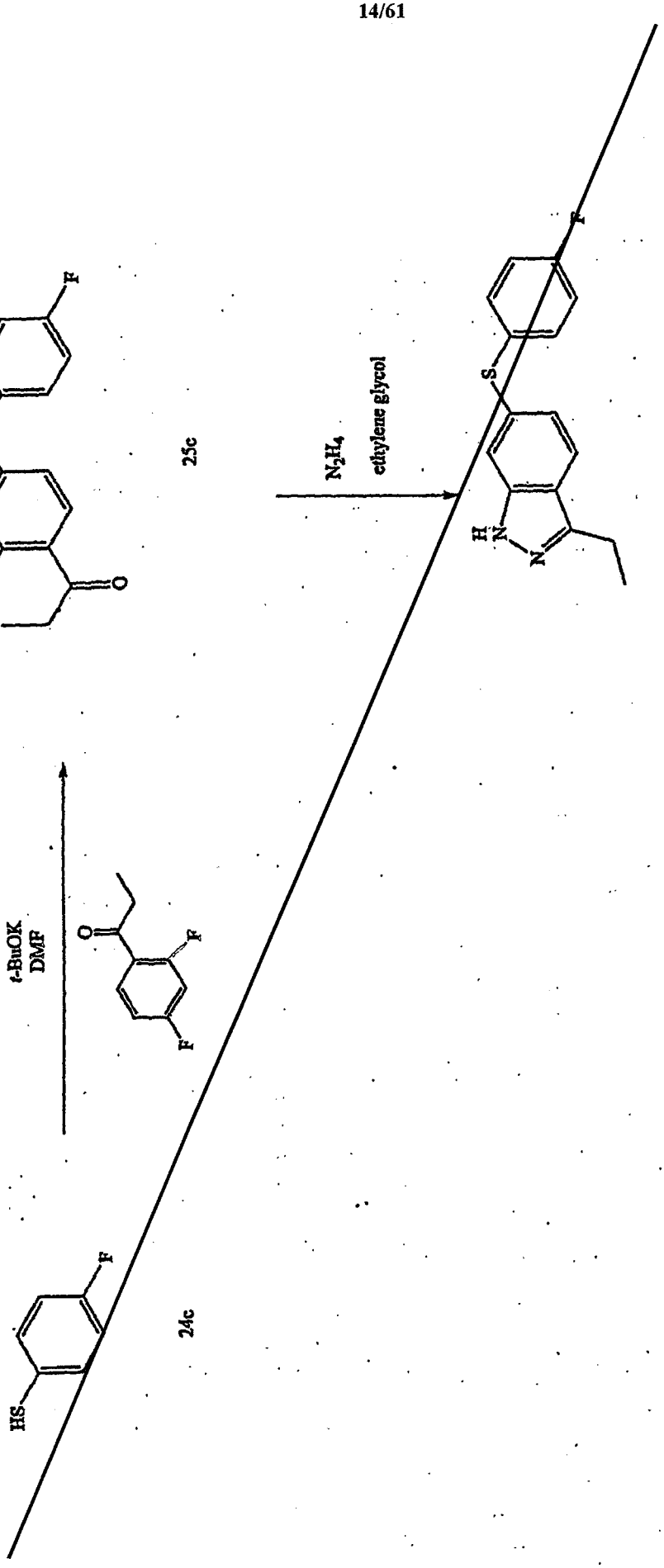


FIG. 13

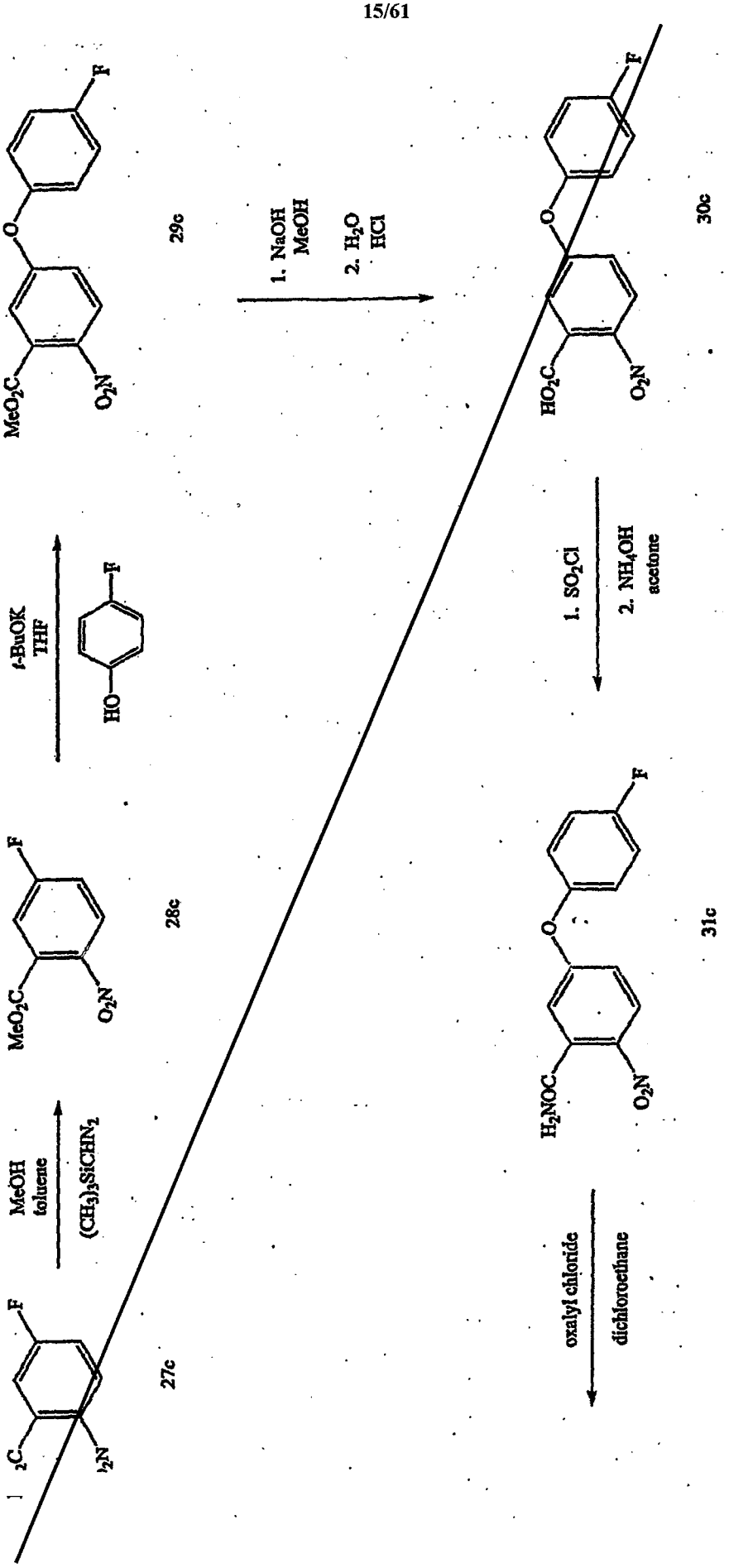

MeOH
toluene
(CH3)3SiCHN2
t-BuOK
THF
1. NaOH
MeOH
2. H2O
HCl
1. SO2Cl
2. NH4OH
acetone
oxalyl chloride
dichloroethane
27c
28c
29c
30c
31c

FIG. 14A

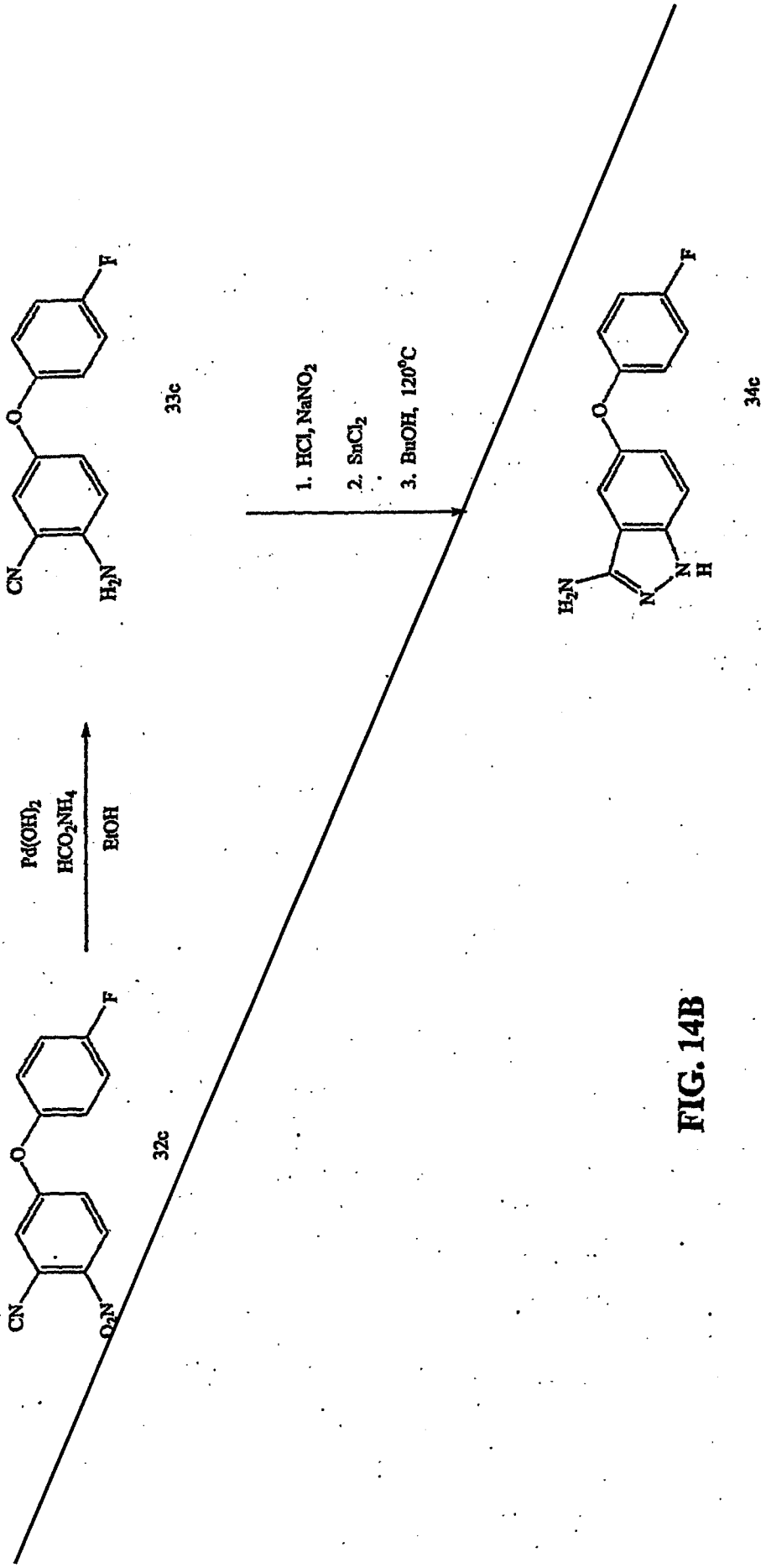

F
O
CN
O2N
32c
Pd(OH)2
HCO2NH4
EtOH
F
O
CN
H2N
33c
1. HCl, NaNO2
2. SnCl2
3. BuOH, 120°C
F
O
H2N
N
N
H
34c

FIG. 14B

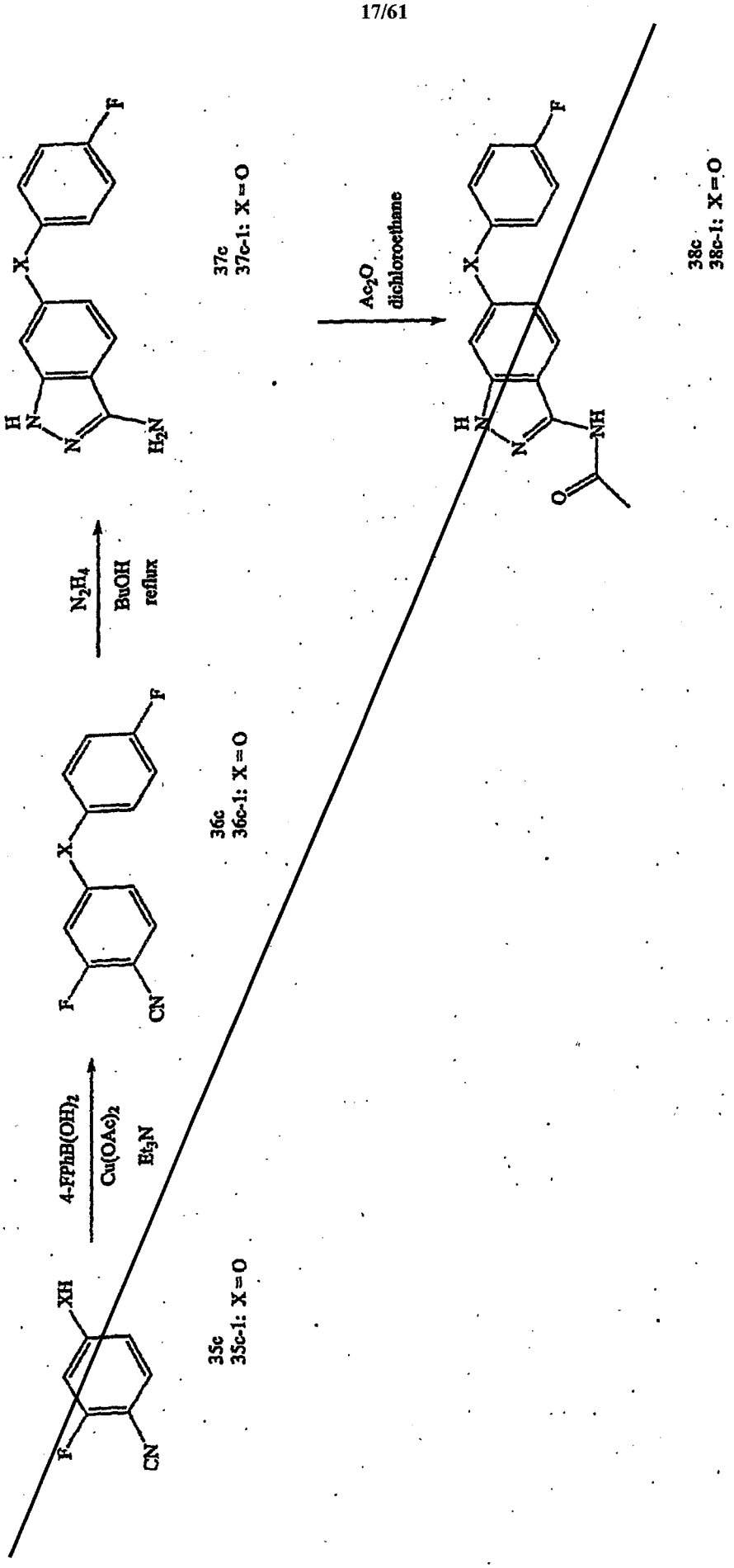

35c
35c-1: X = O
4-FPhB(OH)2
Cu(OAc)2
Et3N
36c
36c-1: X = O
N2H4
BuOH
reflux
37c
37c-1: X = O
Ac2O
dichloroethane
38c
38c-1: X = O

FIG. 15

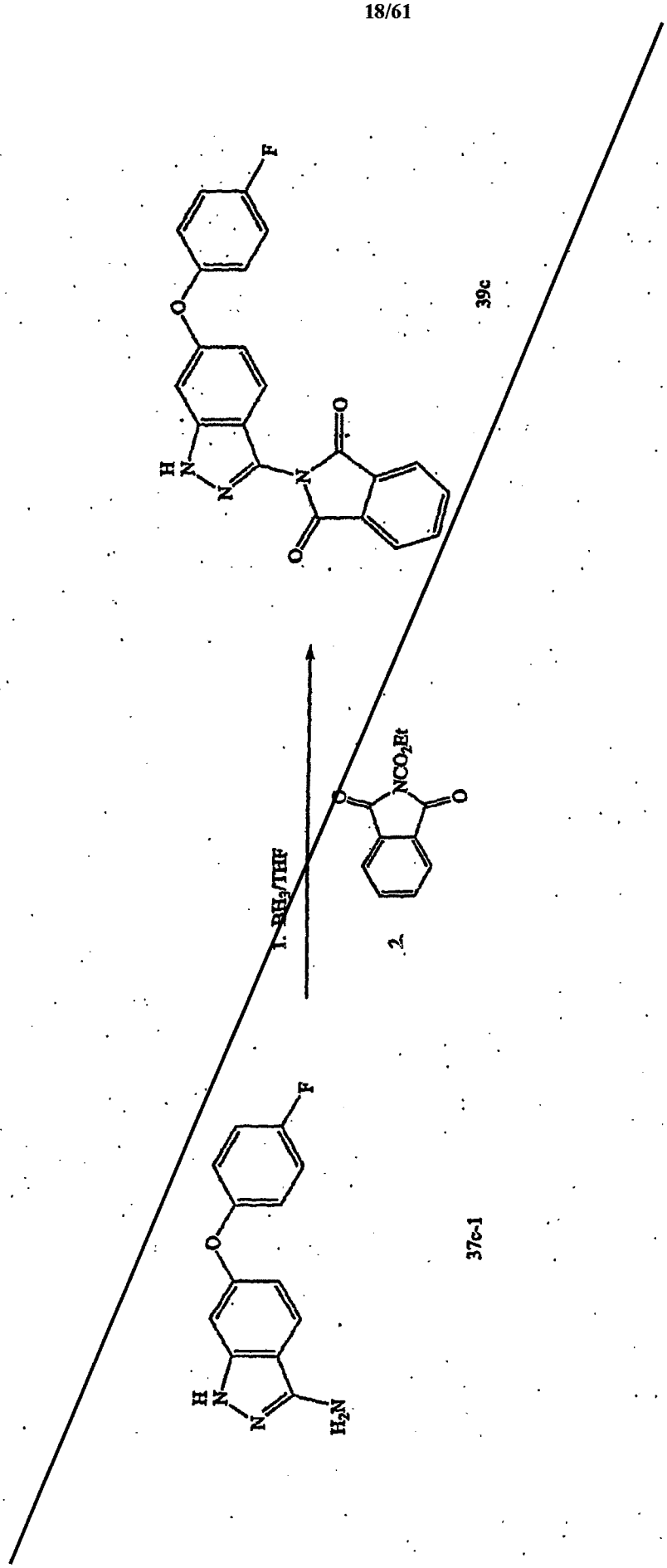


FIG. 16

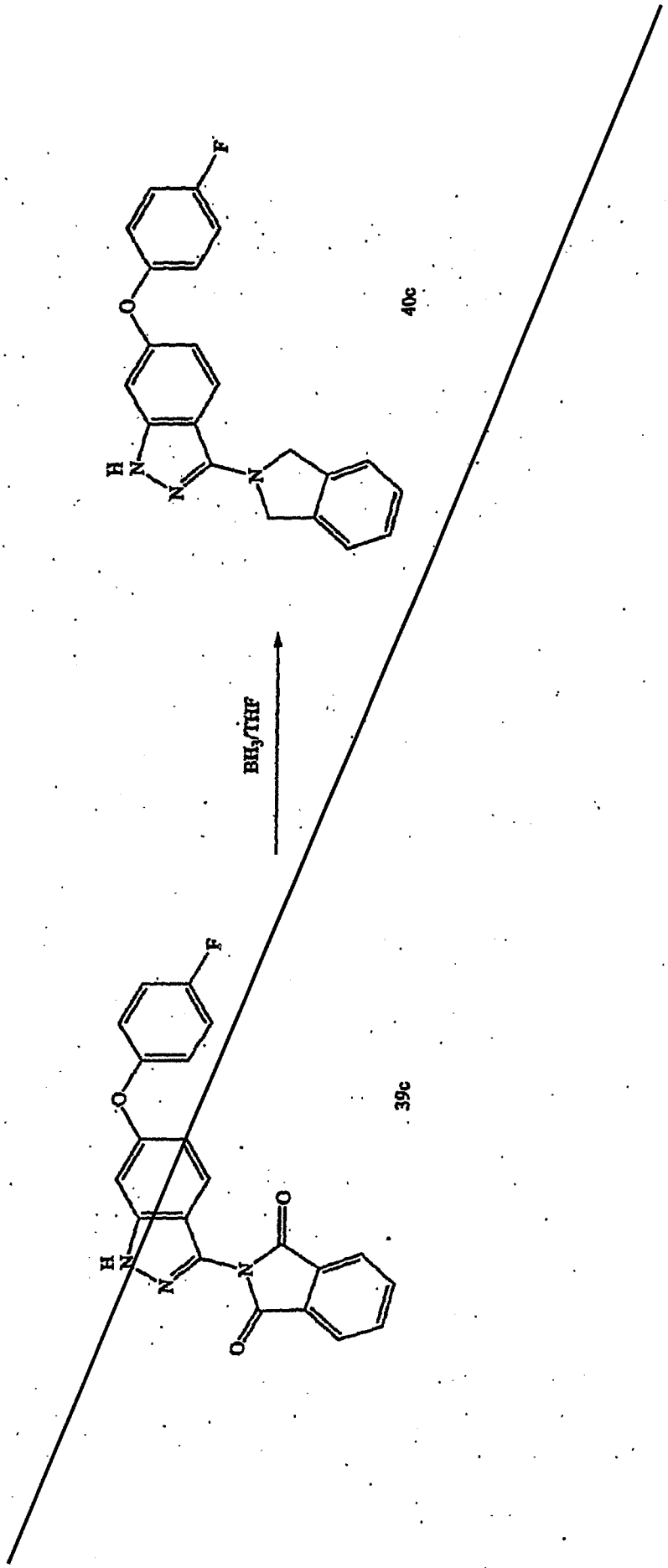


FIG. 17

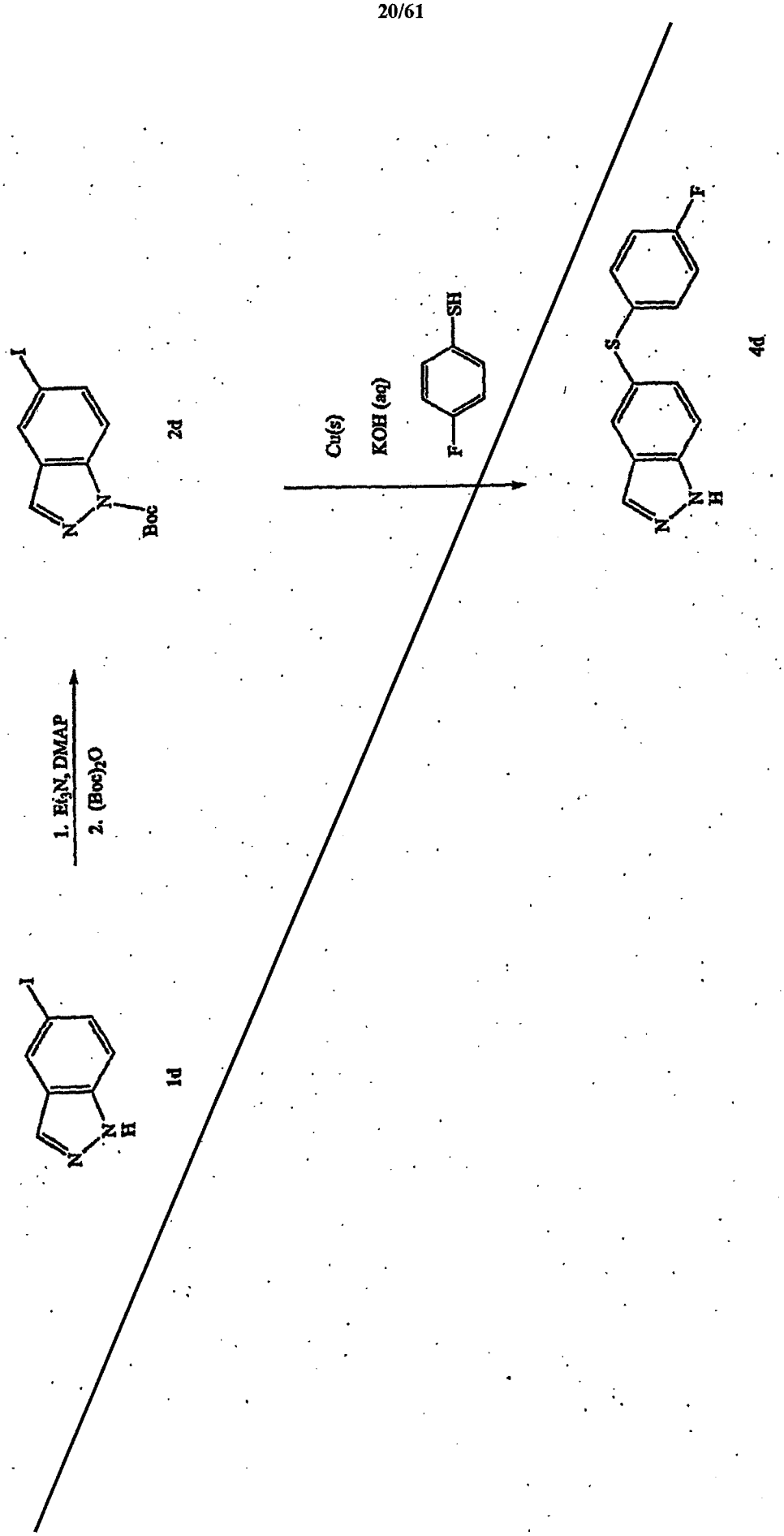


FIG. 18

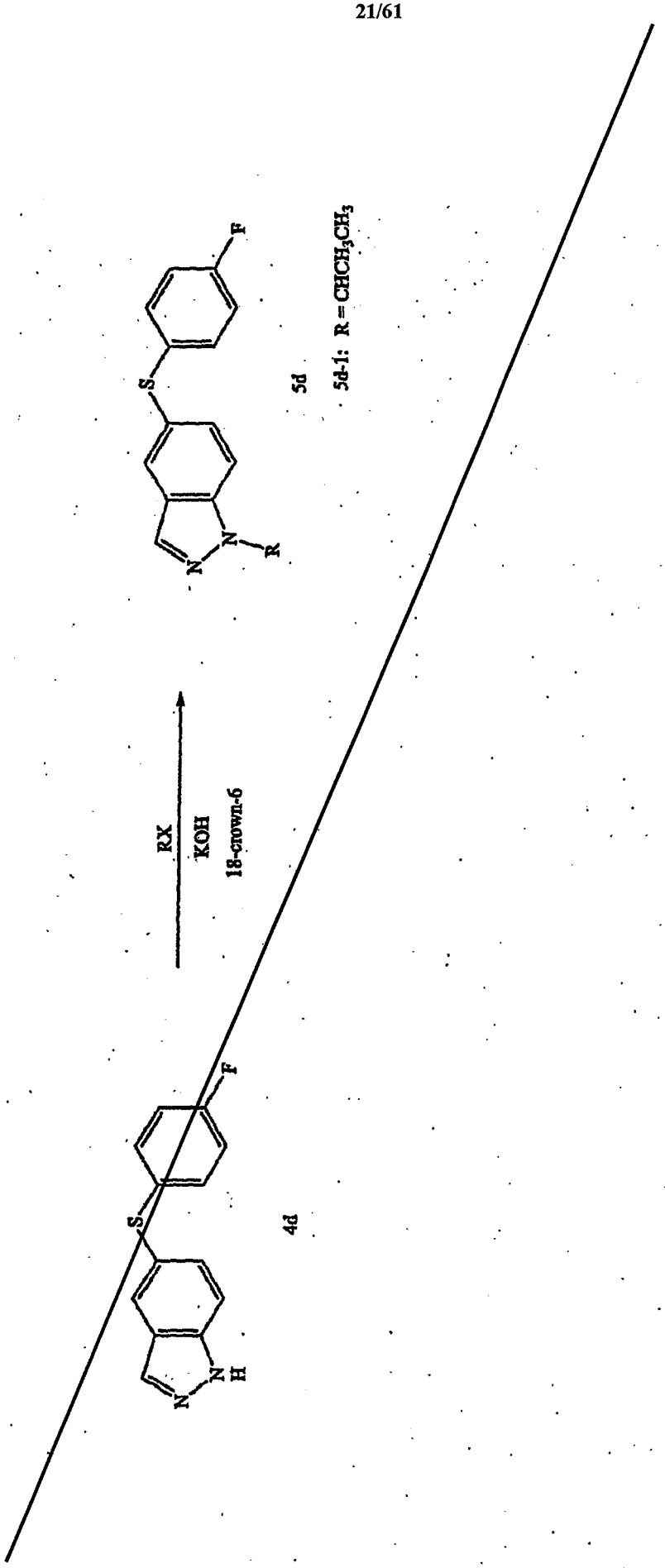


FIG. 19

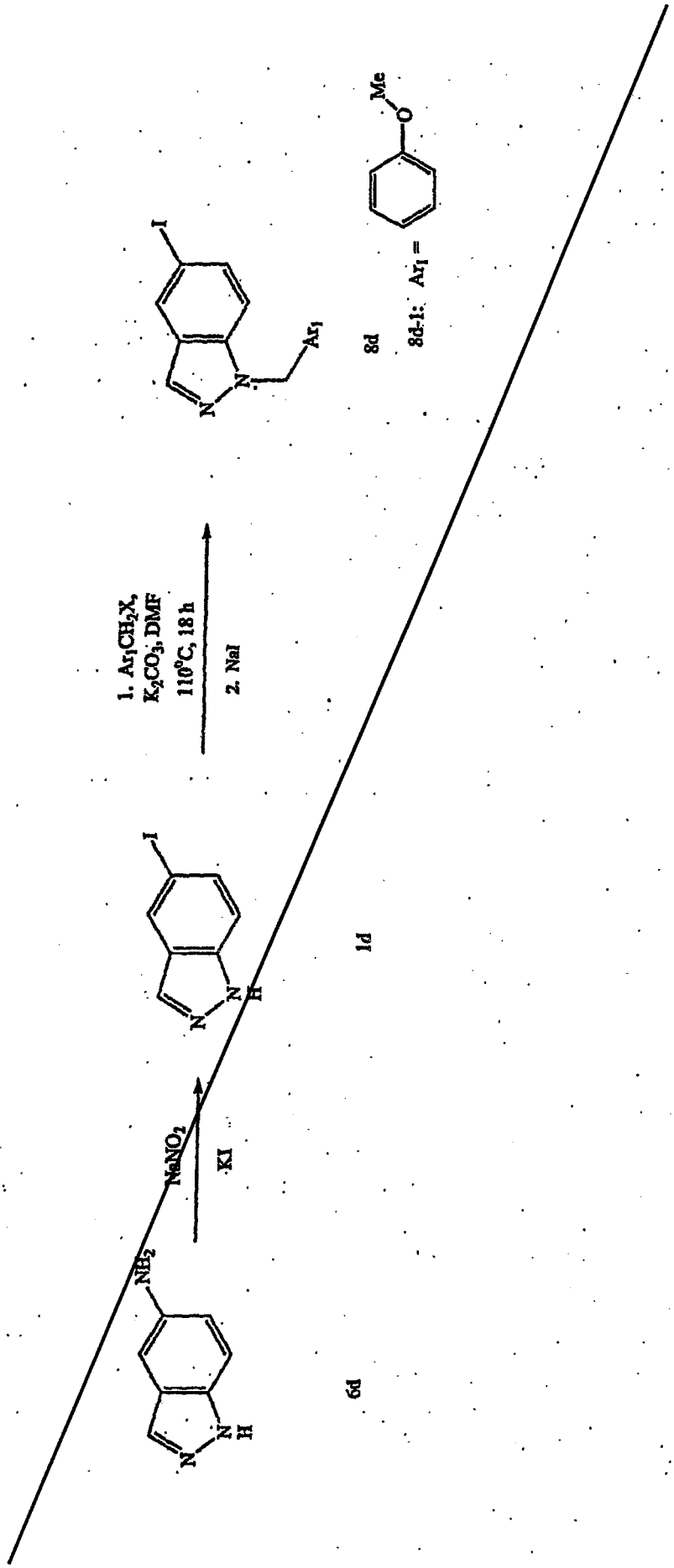


FIG. 20

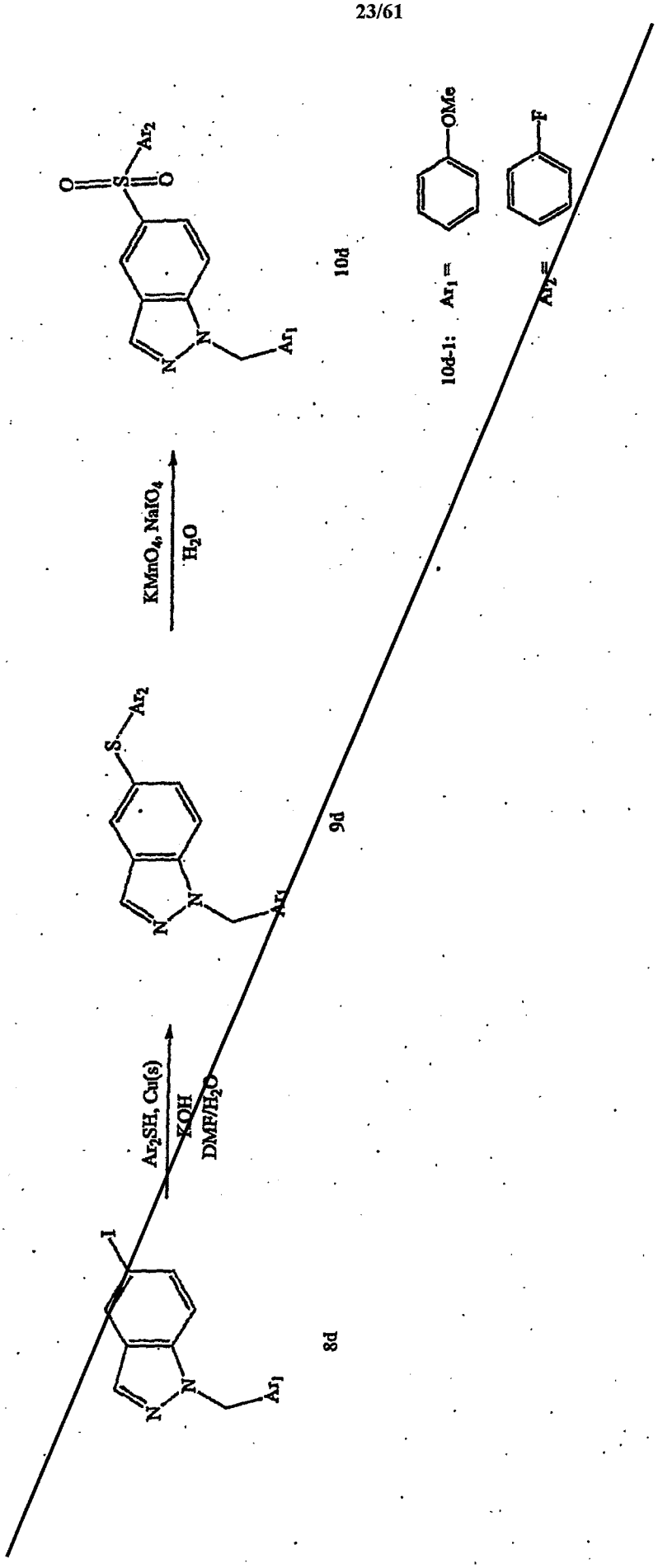

8d
Ar_2SH, Cu(s)
KOH
DMF/H_2O
9d
$KMnO_4$, $NaIO_4$
H_2O
10d
10d-1: Ar_1 =
Ar_2 =
OMe
F

FIG. 21

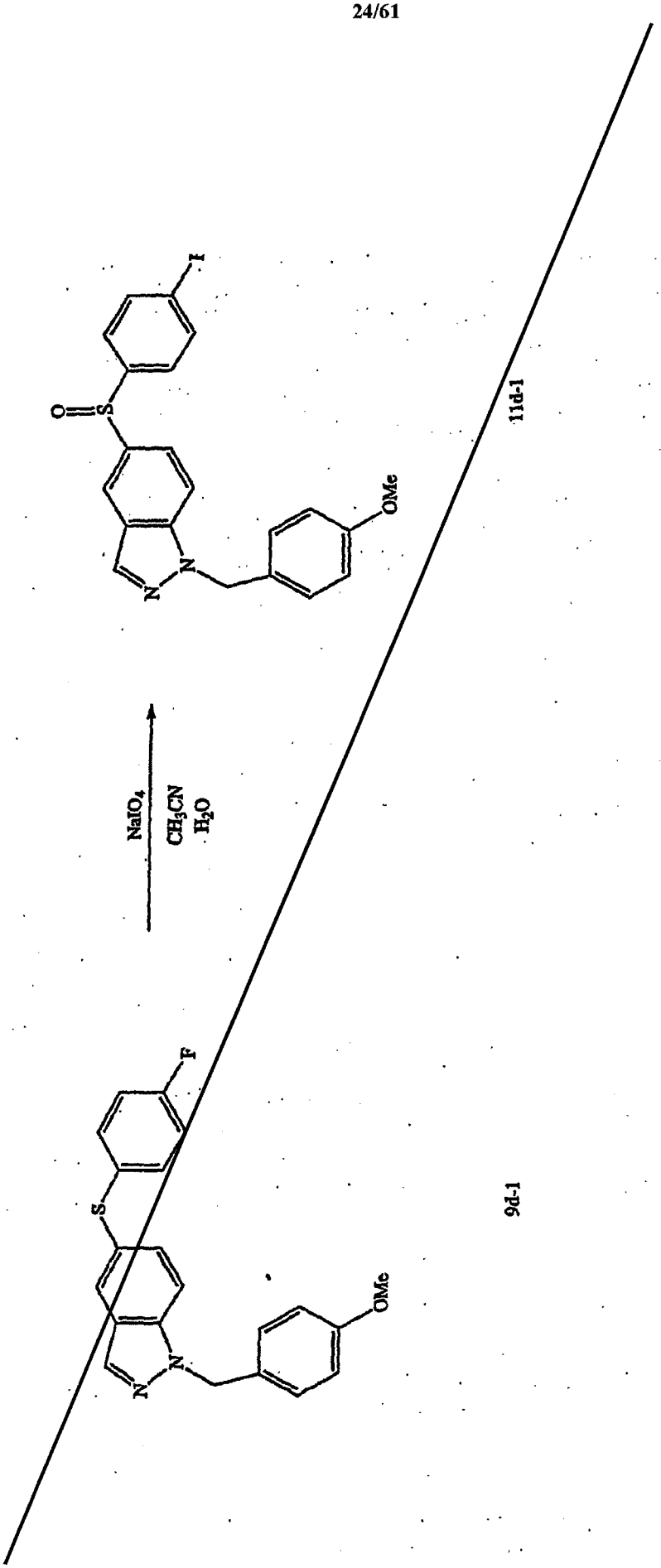


FIG. 22

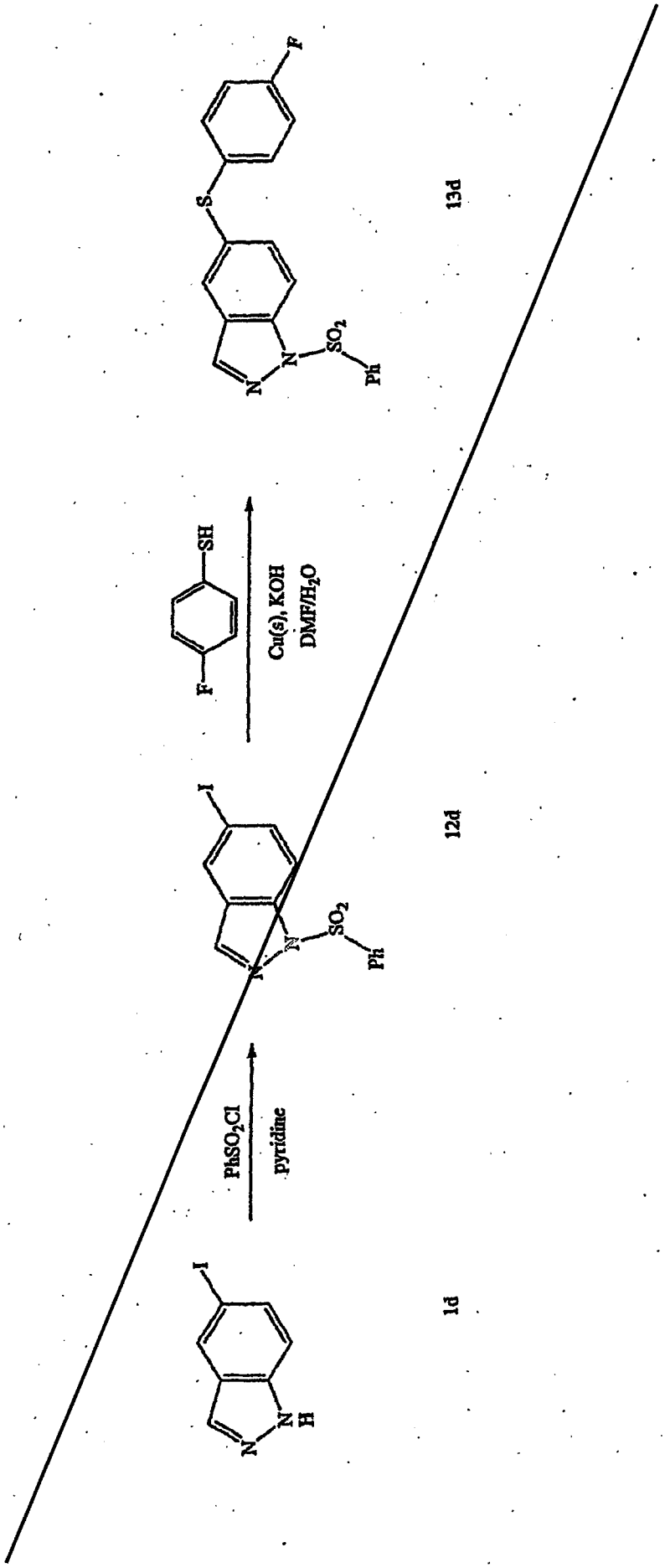


FIG. 23

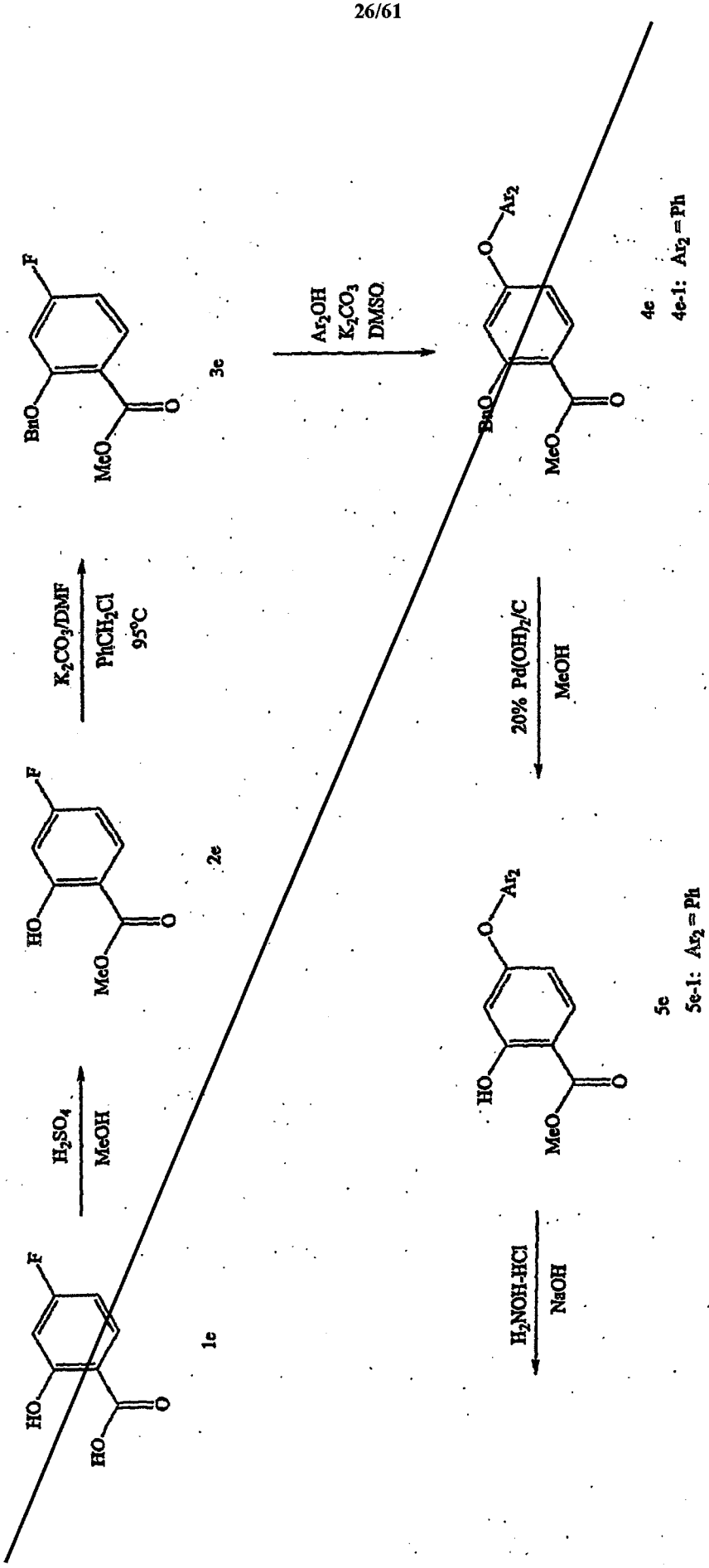

1e
H_2SO_4
MeOH
2e
K_2CO_3/DMF
$PhCH_2Cl$
95°C
3e
Ar_2OH
K_2CO_3
DMSO
4e
4e-1: Ar_2 = Ph
20% $Pd(OH)_2$/C
MeOH
5e
5e-1: Ar_2 = Ph
H_2NOH-HCl
NaOH

FIG. 24A

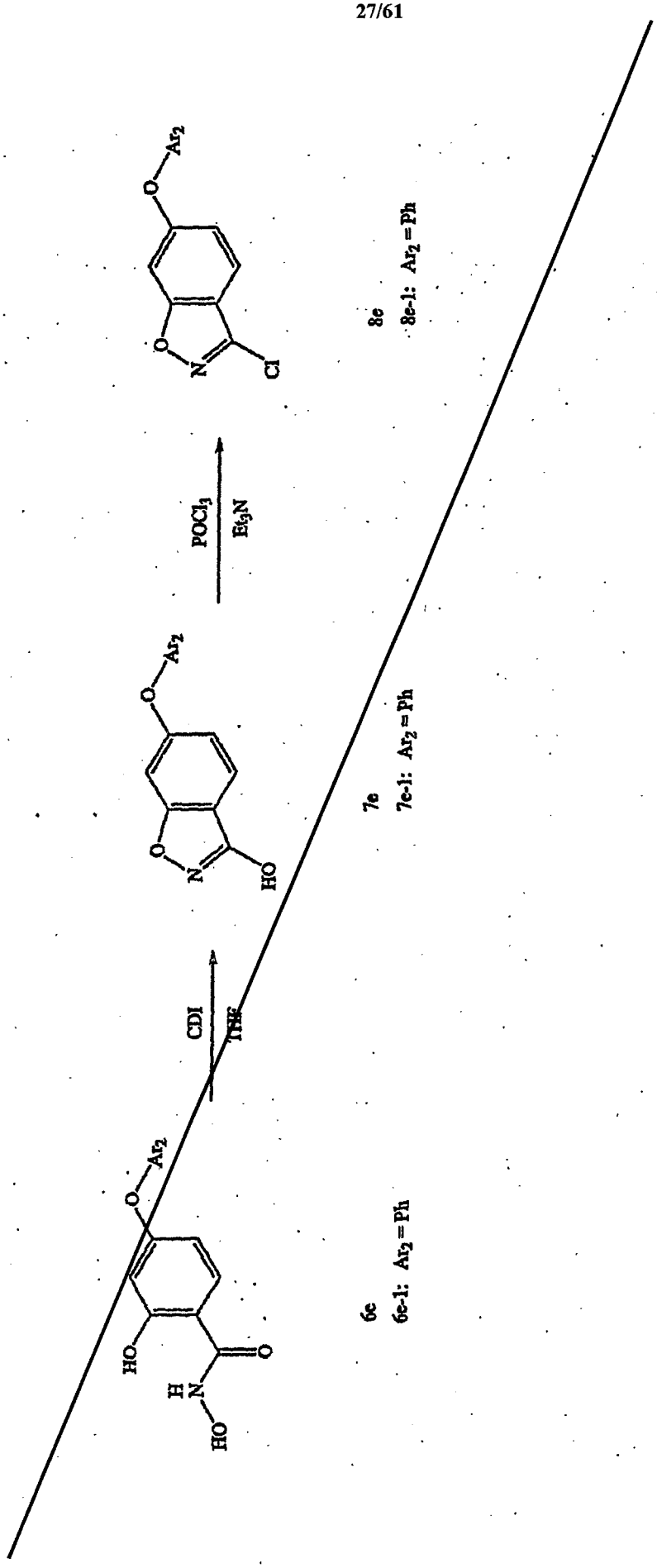


FIG. 24B

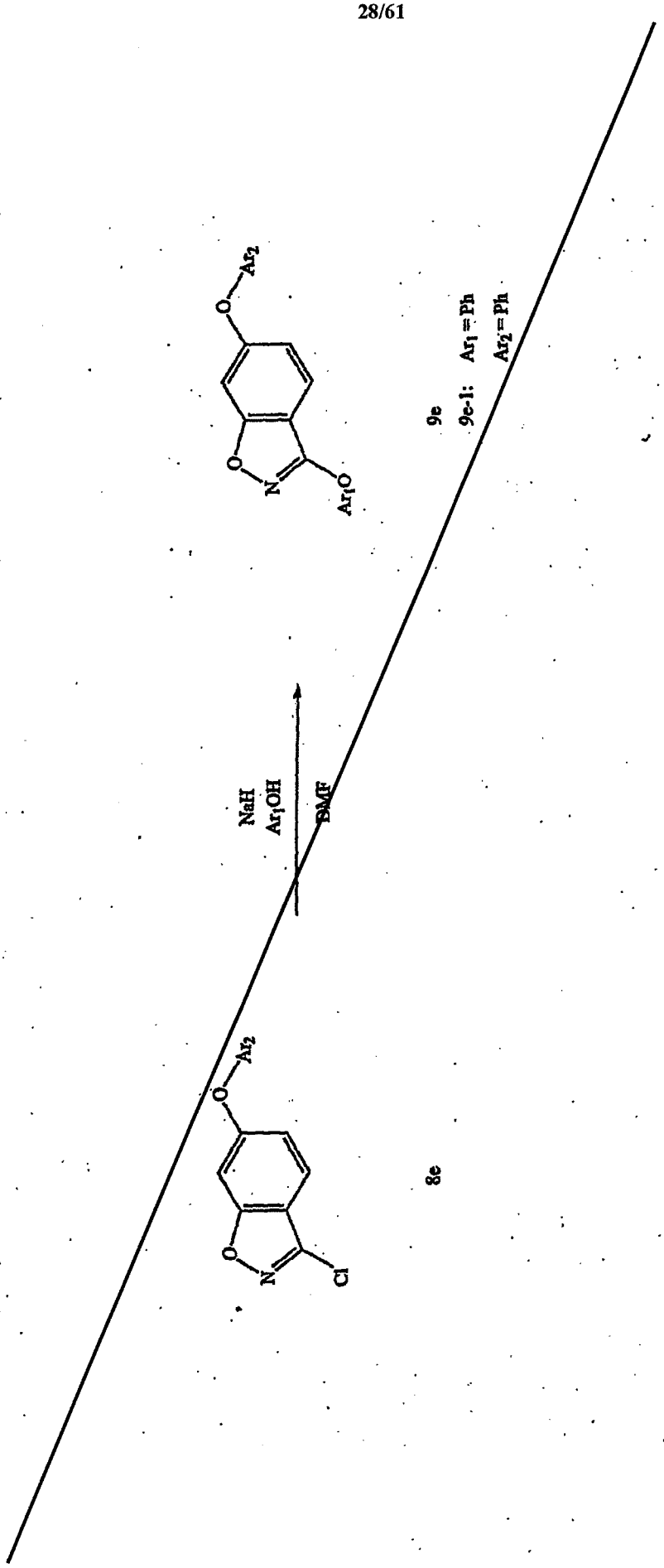


FIG. 25

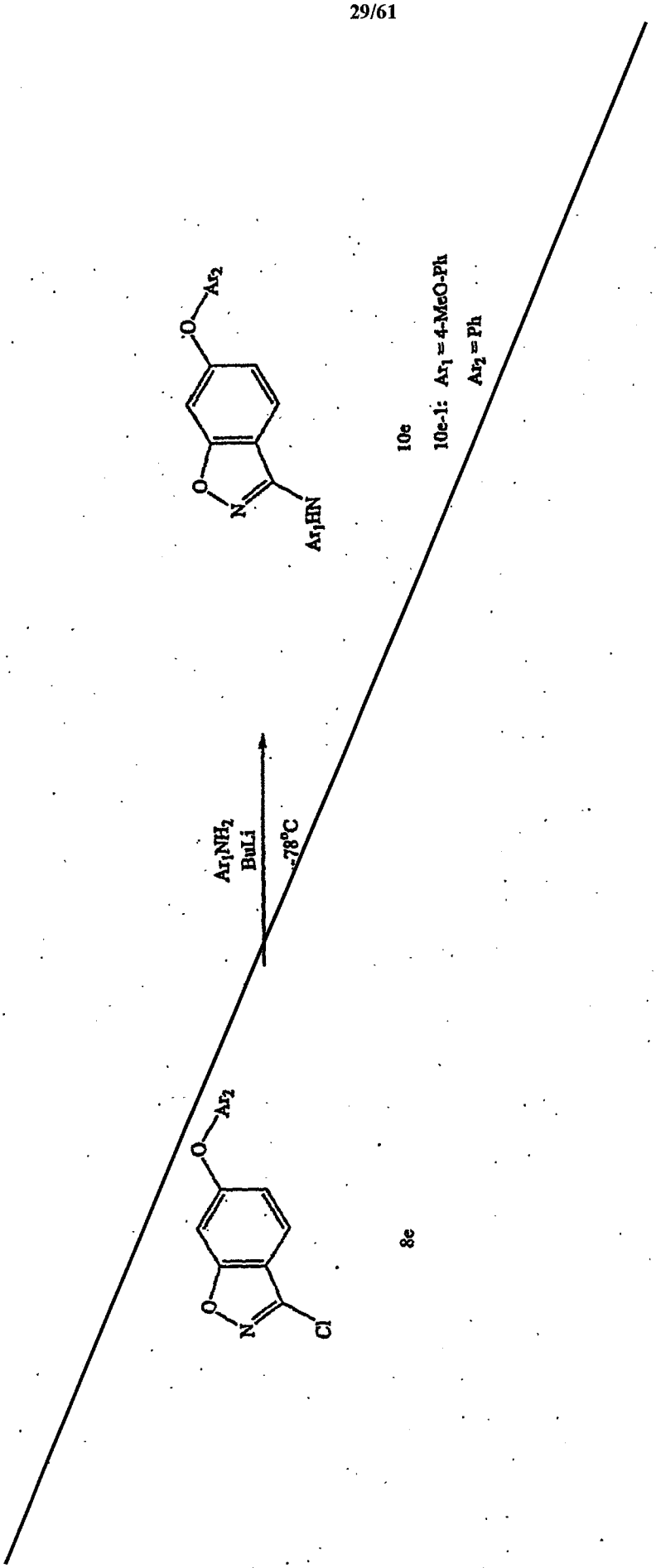
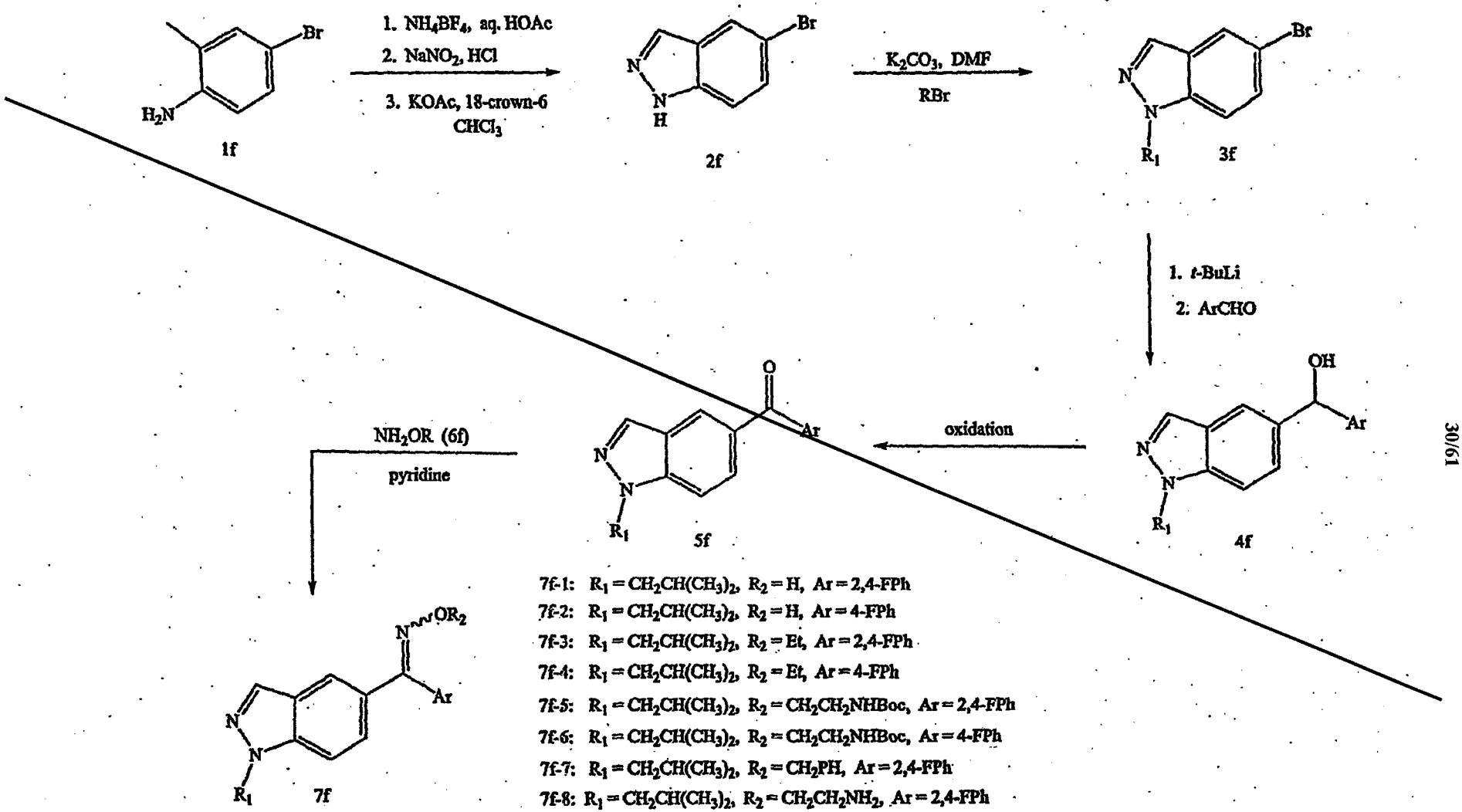
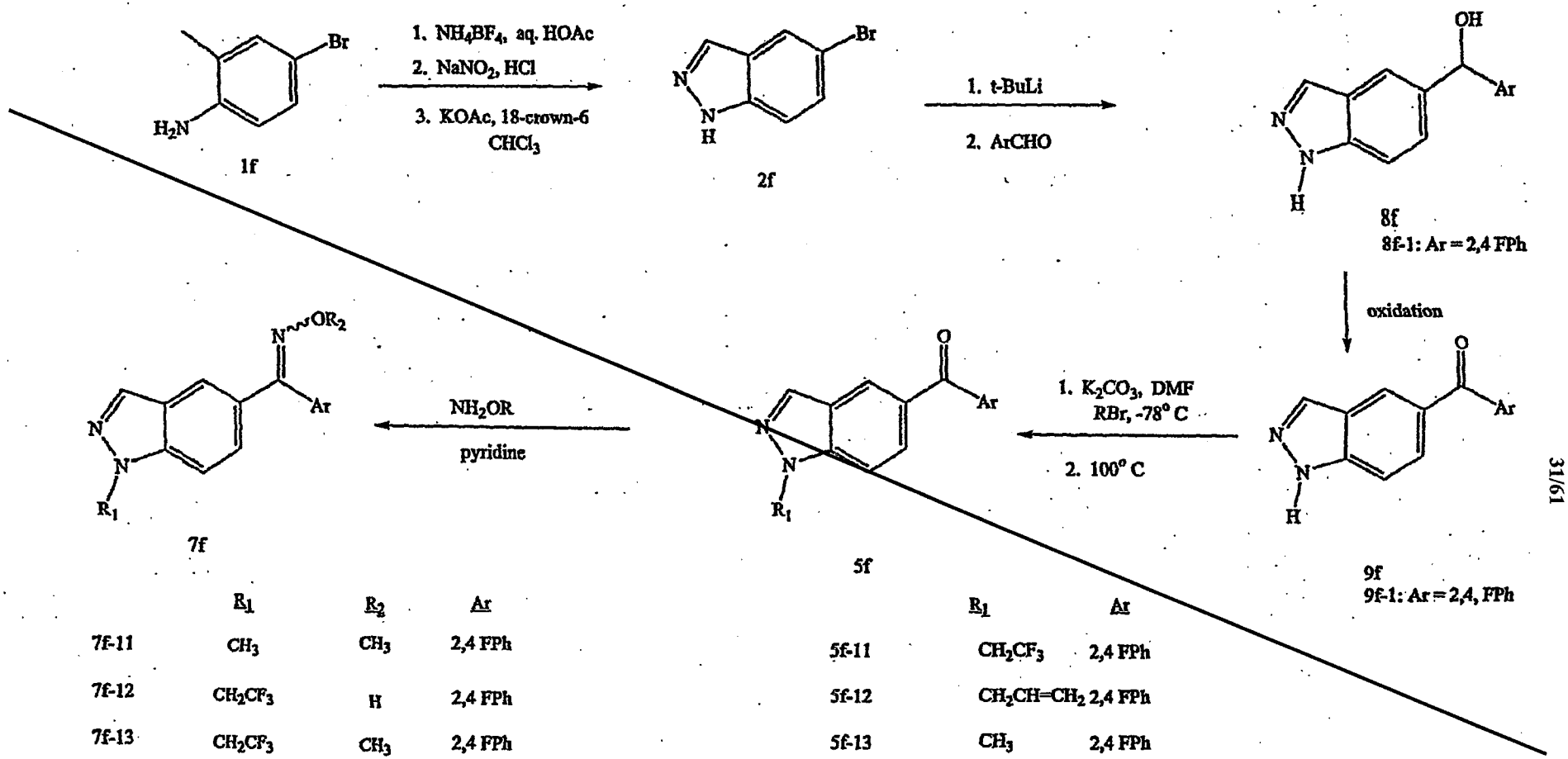

Ar2
O
O
N
Ar1HN
10e
10e-1: Ar1 = 4-MeO-Ph
Ar2 = Ph
Ar1NH2
BuLi
-78°C
Ar2
O
O
N
Cl
8e

FIG. 26



7f-1: $R_1 = CH_2CH(CH_3)_2$, $R_2 = H$, Ar = 2,4-FPh
7f-2: $R_1 = CH_2CH(CH_3)_2$, $R_2 = H$, Ar = 4-FPh
7f-3: $R_1 = CH_2CH(CH_3)_2$, $R_2 = Et$, Ar = 2,4-FPh
7f-4: $R_1 = CH_2CH(CH_3)_2$, $R_2 = Et$, Ar = 4-FPh
7f-5: $R_1 = CH_2CH(CH_3)_2$, $R_2 = CH_2CH_2NHBoc$, Ar = 2,4-FPh
7f-6: $R_1 = CH_2CH(CH_3)_2$, $R_2 = CH_2CH_2NHBoc$, Ar = 4-FPh
7f-7: $R_1 = CH_2CH(CH_3)_2$, $R_2 = CH_2PH$, Ar = 2,4-FPh
7f-8: $R_1 = CH_2CH(CH_3)_2$, $R_2 = CH_2CH_2NH_2$, Ar = 2,4-FPh
7f-9: $R_1 = CH_2CH(CH_3)_2$, $R_2 = Me$, Ar = 4-FPh
7f-10: $R_1 = CH_2CH(CH_3)_2$, $R_2 = CH_2CH_2NH$, Ar = 4-FPh

FIG. 27



	R_1	R_2	Ar
7f-11	CH_3	CH_3	2,4 FPh
7f-12	CH_2CF_3	H	2,4 FPh
7f-13	CH_2CF_3	CH_3	2,4 FPh
7f-14	SO_2Me	H	2,4 FPh
7f-15	SO_2Me	CH_3	2,4 FPh
7f-16	H	CH_3	2,4 FPh
7f-17	$CH_2CH=CH_2$	H	2,4 FPh
7f-18	$CH_2CH=CH_2$	CH_3	2,4 FPh

	R_1	Ar
5f-11	CH_2CF_3	2,4 FPh
5f-12	$CH_2CH=CH_2$	2,4 FPh
5f-13	CH_3	2,4 FPh
5f-14	SO_2Me	2,4 FPh

FIG. 28

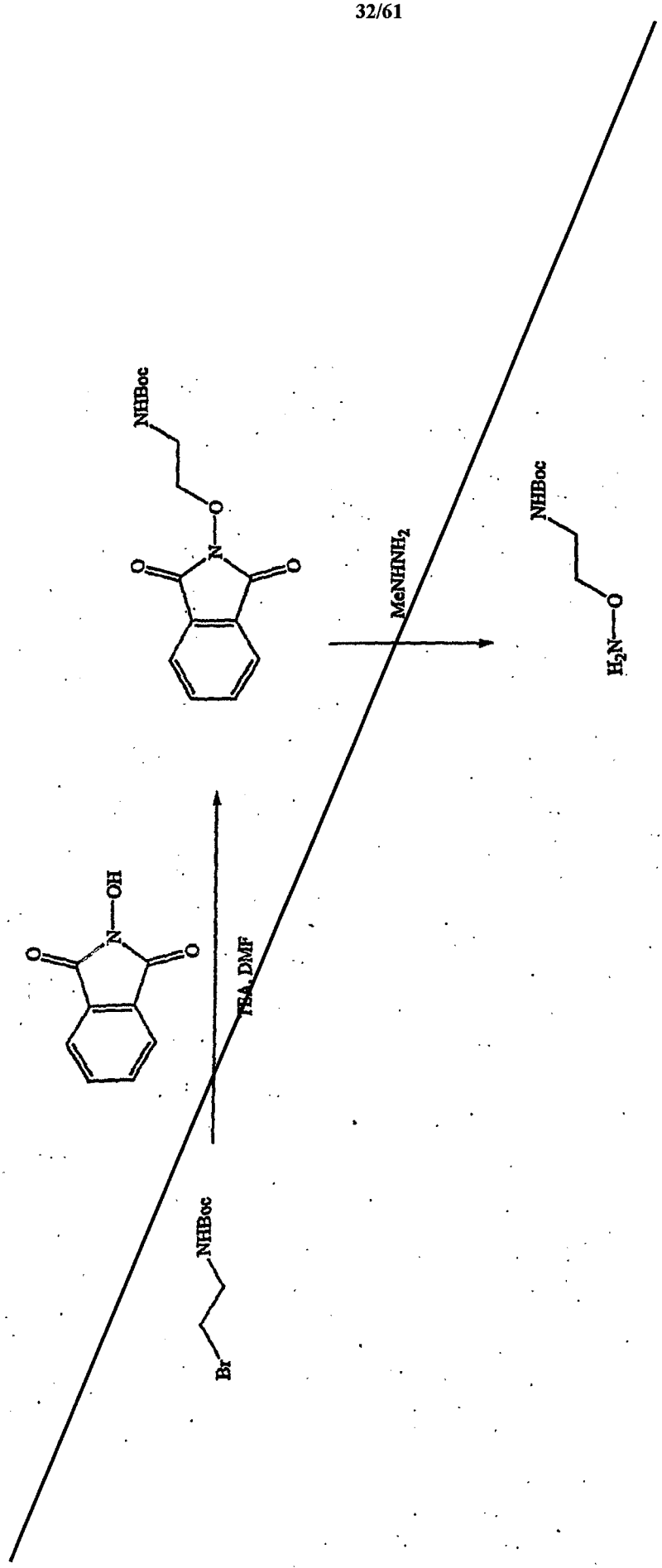


FIG. 29

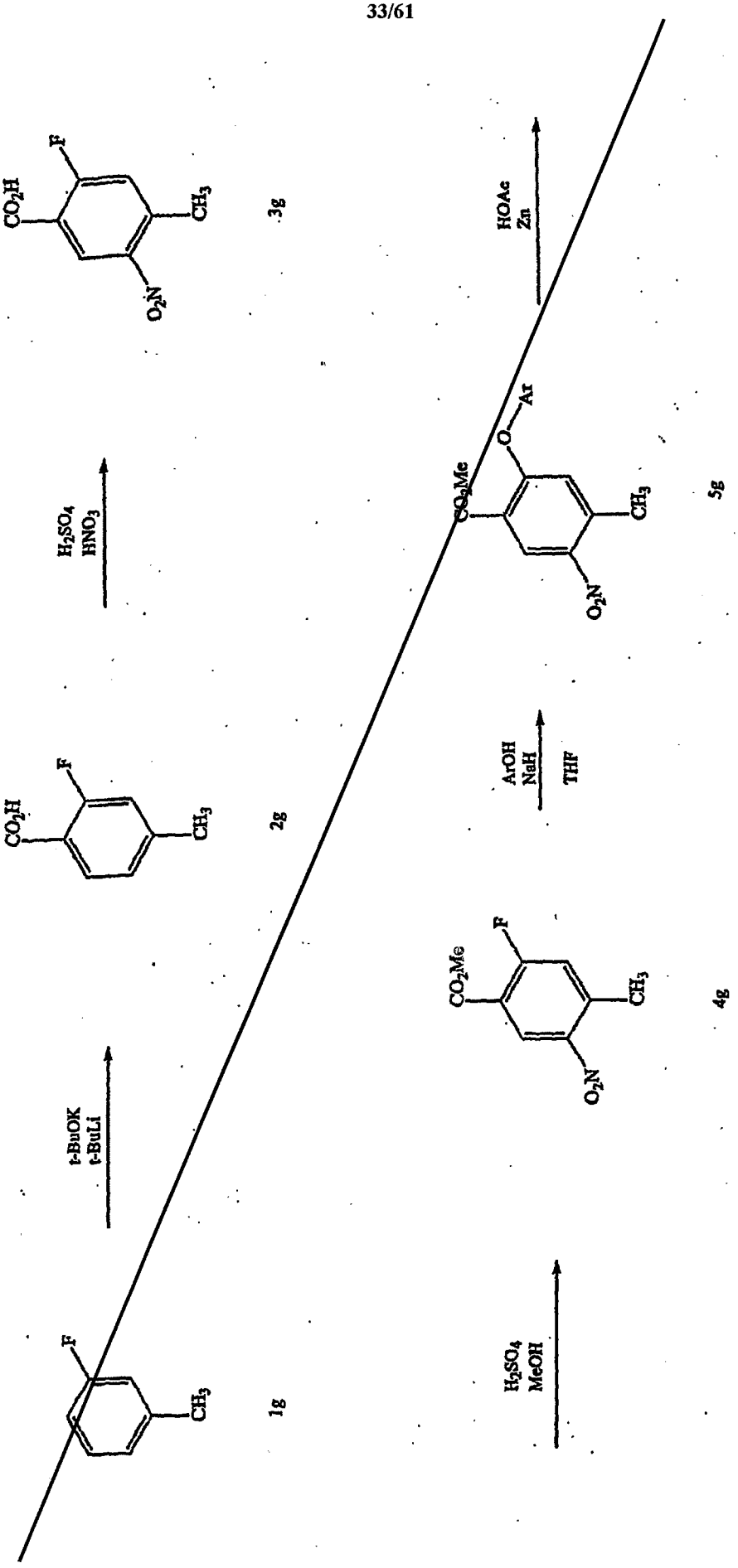

t-BuOK
t-BuLi
H2SO4
HNO3
ArOH
NaH
THF
HOAc
Zn
H2SO4
MeOH
1g
2g
3g
4g
5g

FIG. 30A

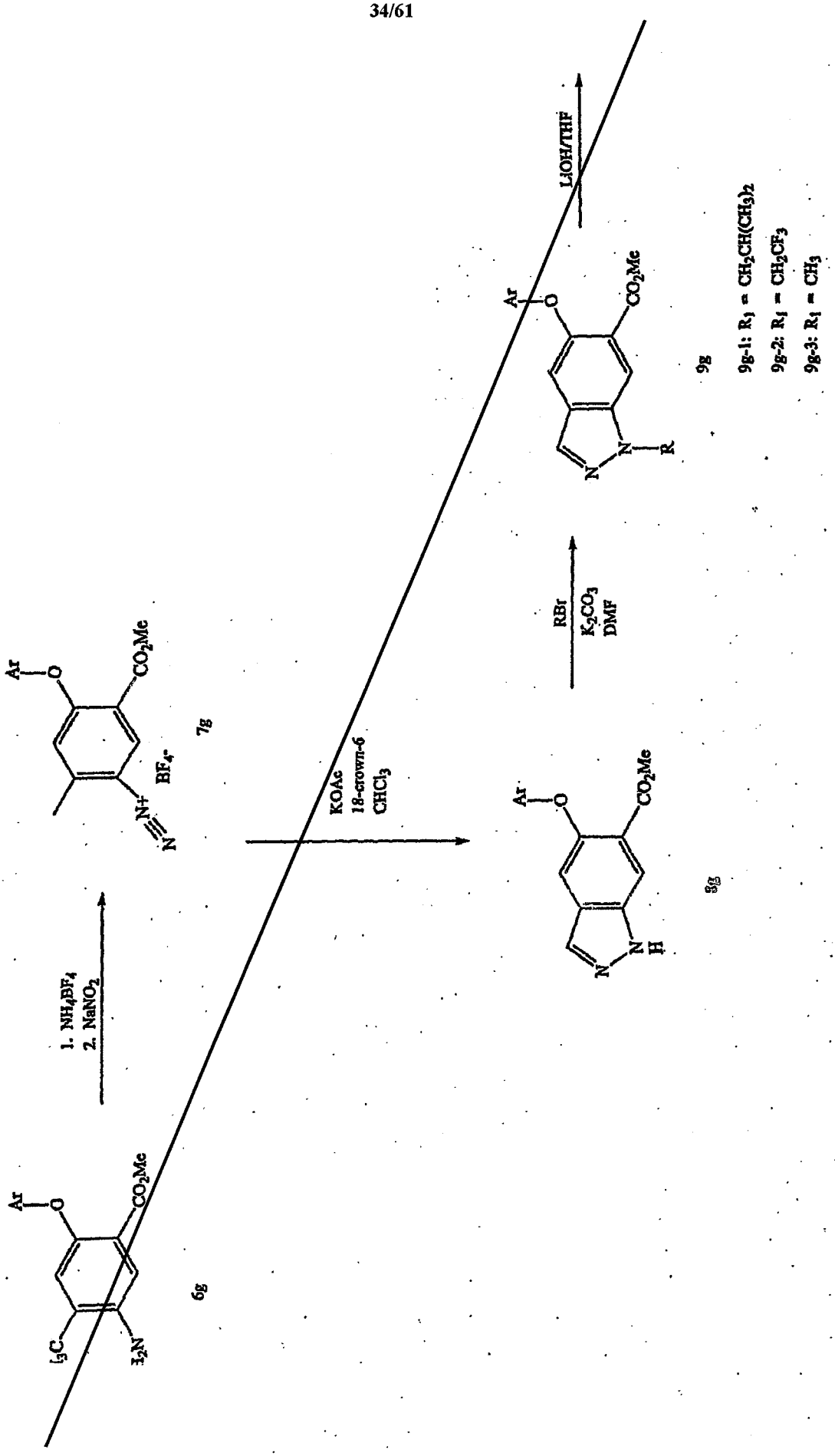
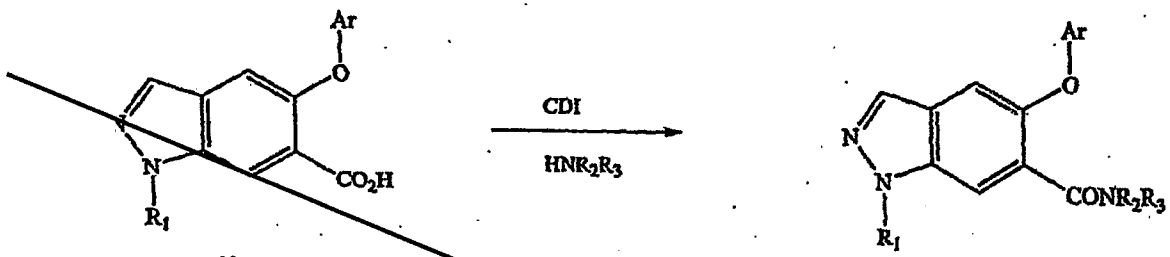

1. NH4BF4
2. NaNO2
KOAc
18-crown-6
CHCl3
RBr
K2CO3
DMF
LiOH/THF
6g
7g
8g
9g
9g-1: R1 = CH2CH(CH3)2
9g-2: R1 = CH2CF3
9g-3: R1 = CH3

FIG. 30B



10g

11g

10g-1: $R_1 = CH_2CH(CH_3)_2$

10g-2: $R_1 = CH_2CF_3$

10g-3: $R_1 = CH_3$

10g-4: $R_1 = H$

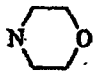
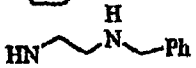
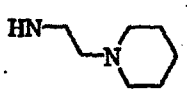
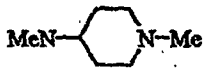
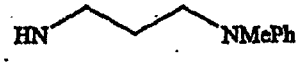
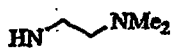
	R_1	NR_2R_3
11g-1:	$CH_2CH(CH_3)_3$	NH_2
11g-2:	$CH_2CH(CH_3)_3$	
11g-3:	$CH_2CH(CH_3)_3$	
11g-4:	$CH_2CH(CH_3)_3$	
11g-5:	$CH_2CH(CH_3)_3$	
11g-6:	$CH_2CH(CH_3)_3$	
11g-7:	$CH_2CH(CH_3)_3$	
11g-8:	$CH_2CH(CH_3)_3$	
11g-9:	$CH_2CH(CH_3)_3$	
11g-10:	$CH_2CH(CH_3)_3$	
11g-11:	$CH_2CH(CH_3)_3$	
11g-12:	$CH_2CH(CH_3)_3$	
11g-13:	$CH_2CH(CH_3)_3$	
11g-14:	CH_2CF_3	
11g-15:	CH_3	
11g-16:	H	

FIG. 30C

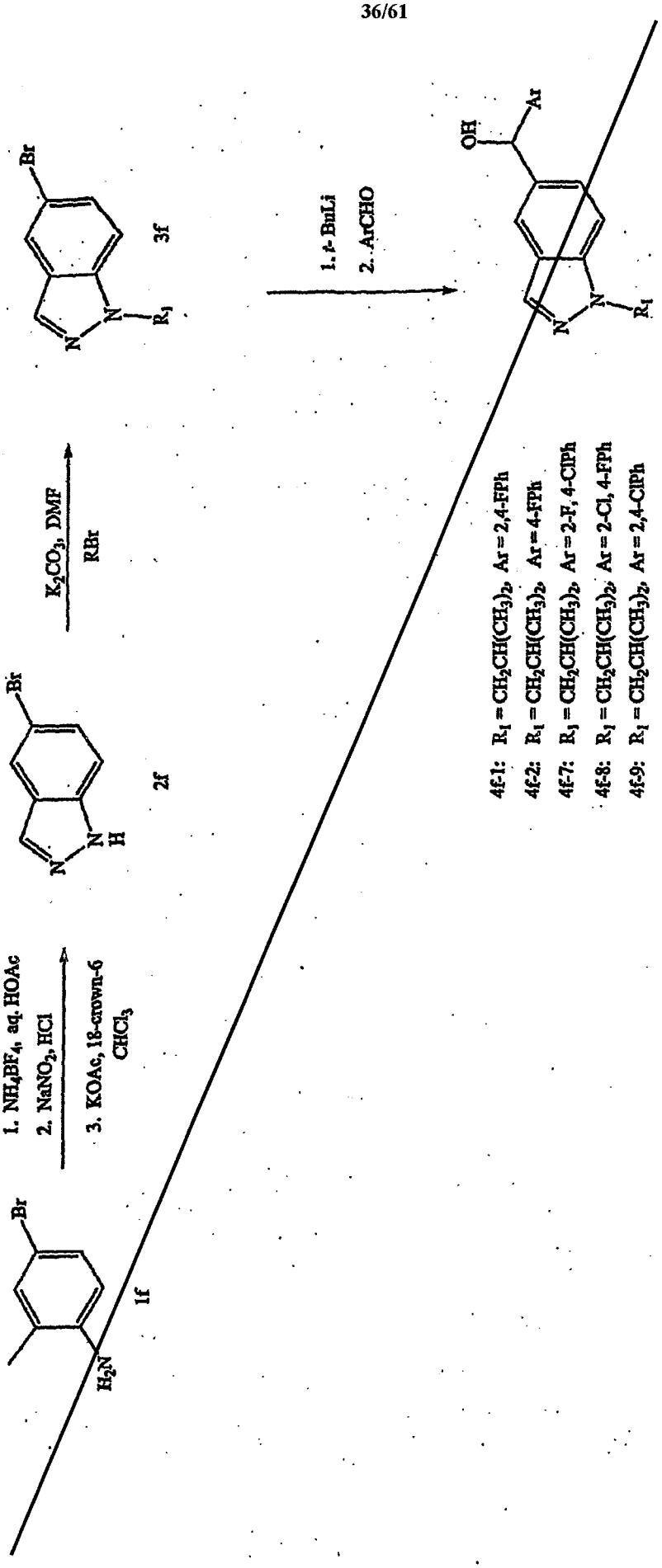
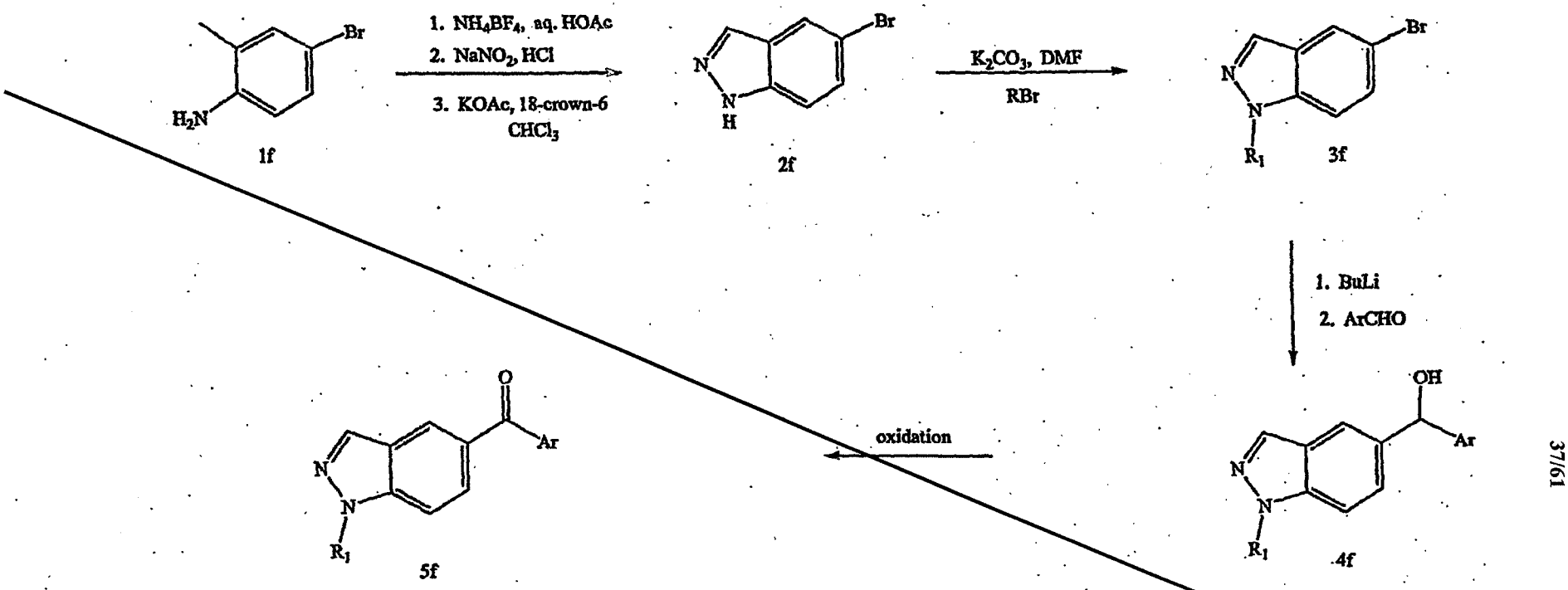

1. NH_4BF_4, aq. HOAc
2. $NaNO_2$, HCl
3. KOAc, 18-crown-6
$CHCl_3$
K_2CO_3, DMF
RBr
1. t- BuLi
2. ArCHO
1f
2f
3f
4f
4f-1: $R_1 = CH_2CH(CH_3)_2$, Ar = 2,4-FPh
4f-2: $R_1 = CH_2CH(CH_3)_2$, Ar = 4-FPh
4f-7: $R_1 = CH_2CH(CH_3)_2$, Ar = 2-F, 4-ClPh
4f-8: $R_1 = CH_2CH(CH_3)_2$, Ar = 2-Cl, 4-FPh
4f-9: $R_1 = CH_2CH(CH_3)_2$, Ar = 2,4-ClPh
4f-10: $R_1 = CH_2CH(CH_3)_2$, Ar = 2-MePh

FIG. 31



5f-1: $R_1 = CH_2CH(CH_3)_2$, Ar = 2,4-FPh
5f-2: $R_1 = CH_2CH(CH_3)_2$, Ar = 4-FPh
5f-7: $R_1 = CH_2CH(CH_3)_2$, Ar = 2-F, 4-ClPh
5f-8: $R_1 = CH_2CH(CH_3)_2$, Ar = 2-Cl, 4-FPh
5f-9: $R_1 = CH_2CH(CH_3)_2$, Ar = 2,4-ClPh
5f-10: $R_1 = CH_2CH(CH_3)_2$, Ar = 2-MePh

4f-1: $R_1 = CH_2CH(CH_3)_2$, Ar = 2,4-FPh
4f-2: $R_1 = CH_2CH(CH_3)_2$, Ar = 4-FPh
4f-7: $R_1 = CH_2CH(CH_3)_2$, Ar = 2-F, 4-ClPh
4f-8: $R_1 = CH_2CH(CH_3)_2$, Ar = 2-Cl, 4-FPh
4f-9: $R_1 = CH_2CH(CH_3)_2$, Ar = 2,4-ClPh
4f-10: $R_1 = CH_2CH(CH_3)_2$, Ar = 2-MePh

FIG. 32

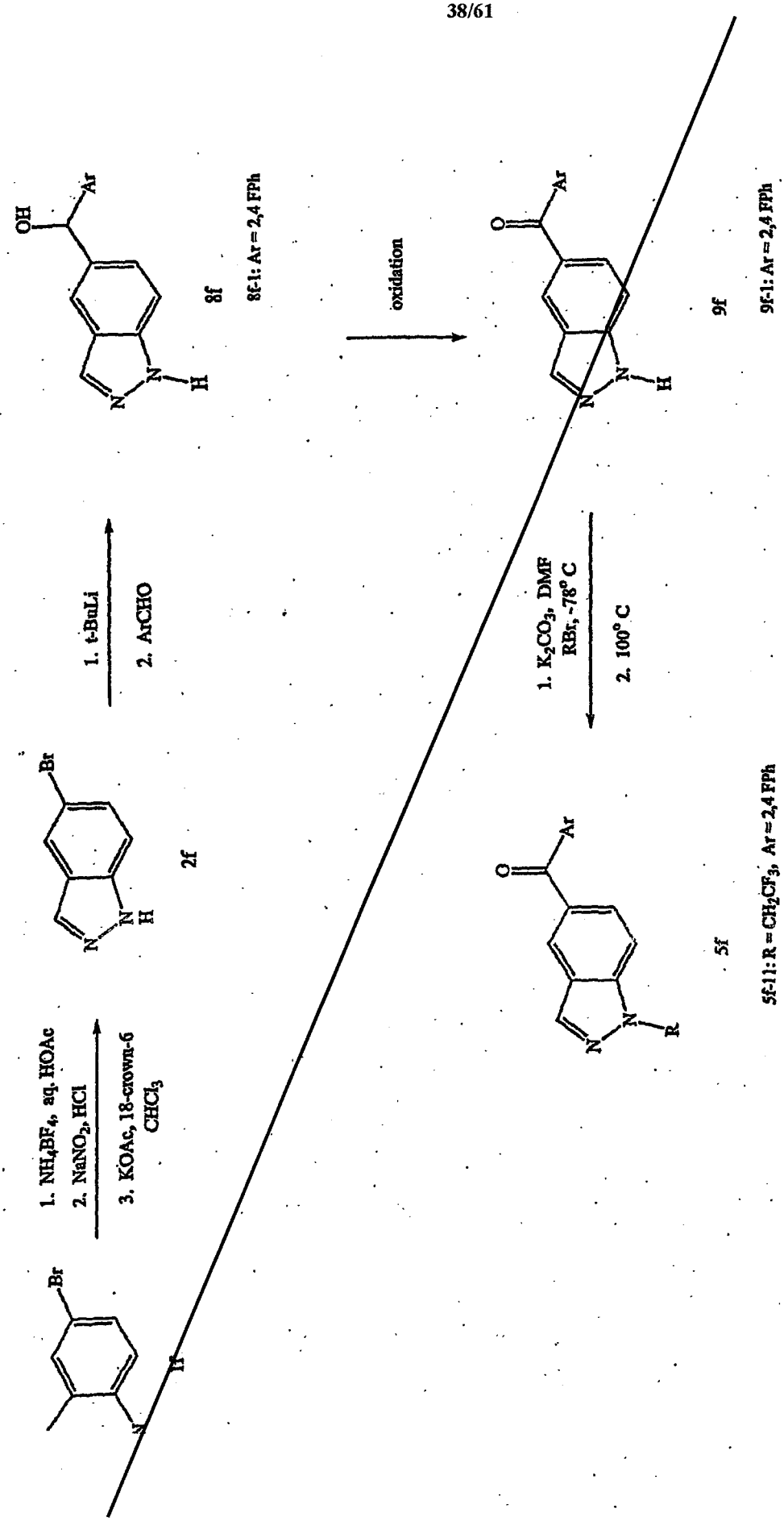
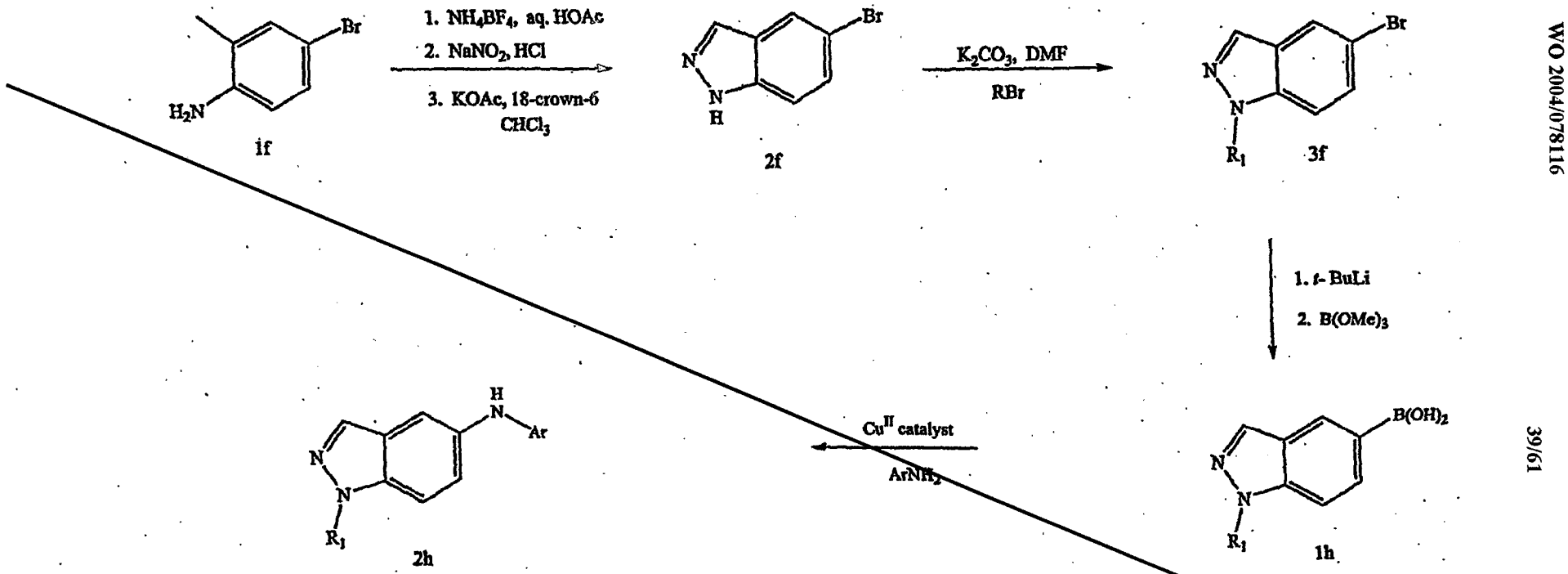

1. NH_4BF_4, aq. HOAc
2. $NaNO_2$, HCl
3. KOAc, 18-crown-6
$CHCl_3$
2f
1. t-BuLi
2. ArCHO
8f
8f-1: Ar = 2,4 FPh
oxidation
9f
9f-1: Ar = 2,4 FPh
1. K_2CO_3, DMF
RBr, -78° C
2. 100° C
5f
5f-11: R = CH_2CF_3, Ar = 2,4 FPh
5f-12: R = $CH_2CH{=}CH_2$, Ar = 2,4 FPh

FIG. 33



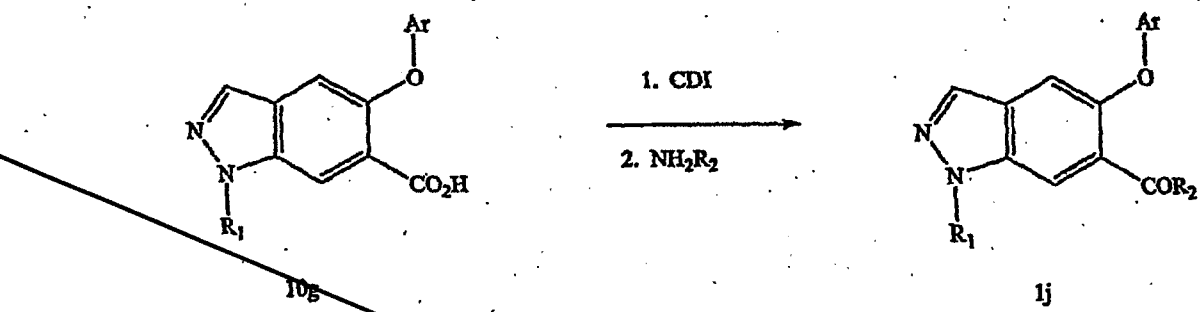
2h-1: $R_1 = CH_2CH(CH_3)_2$, Ar = 2,4-FPh

2h-2: $R_1 = CH_2CH(CH_3)_2$, Ar = 4-FPh

2h-9: $R_1 = CH_2CH(CH_3)_2$, Ar = 2,4-ClPh

2h-10: $R_1 = CH_2CH(CH_3)_2$, Ar = 2-MePh

FIG. 34



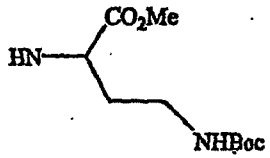
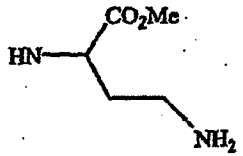
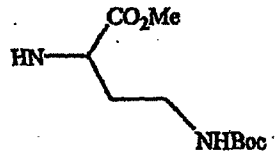
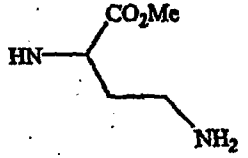
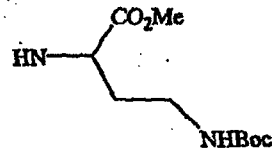
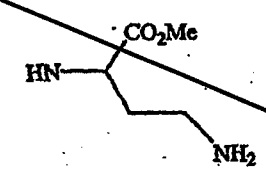
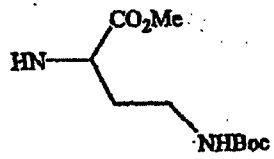
	R1	R2	Ar
1j-1:	H		4-FPh
1j-2:	H		4-FPh
1j-3:	CH_2CF_3		4-FPh
1j-4:	CH_2CF_3		4-FPh
1j-5:	CH_3		4-FPh
1j-6:	CH_3		4-FPh
1j-7:	$CH_2CH(CH_3)_2$		4-FPh

FIG. 35

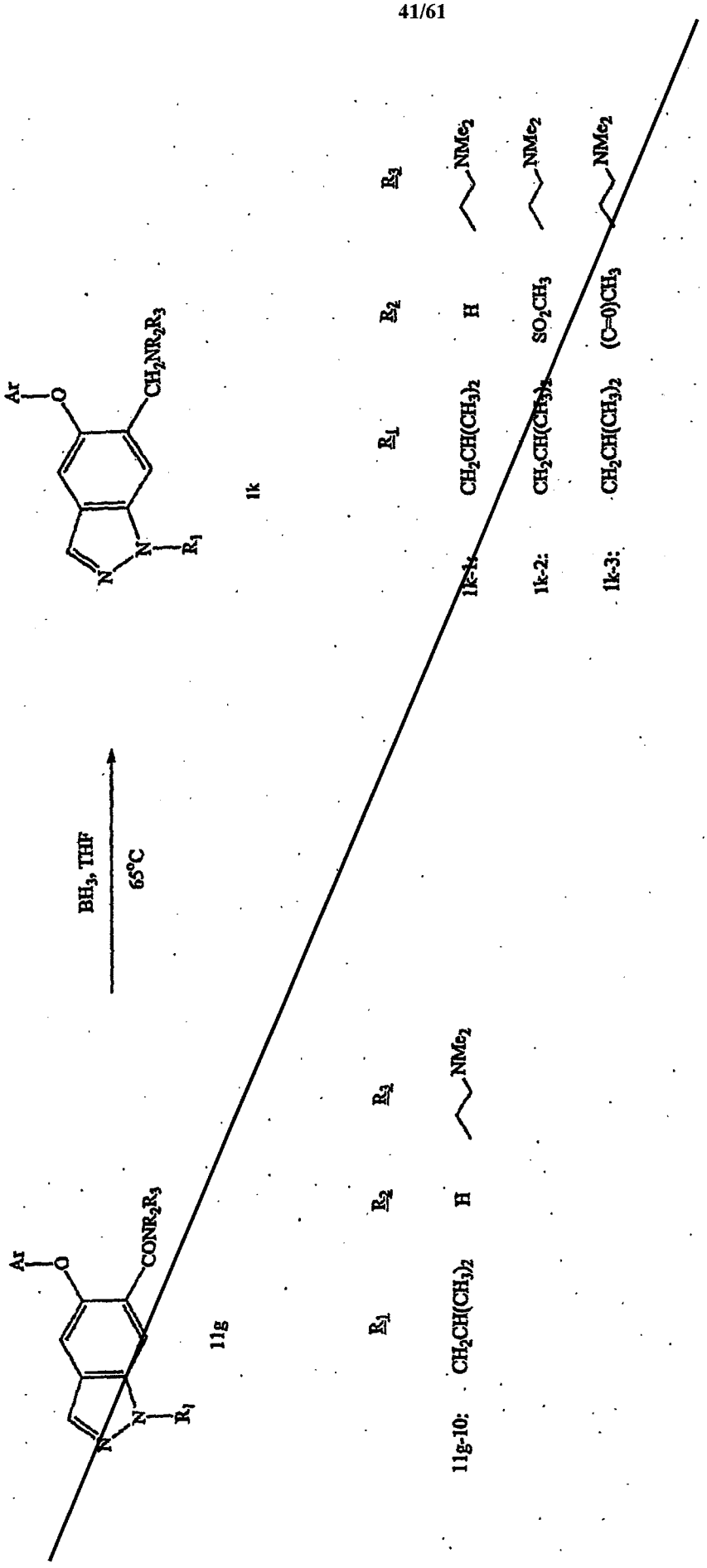

Ar
O
CONR2R3
N
N
R1
11g
BH3, THF
65°C
Ar
O
CH2NR2R3
N
N
R1
1k
R1 R2 R3
11g-10: CH2CH(CH3)2 H NMe2
R1 R2 R3
1k-1: CH2CH(CH3)2 H NMe2
1k-2: CH2CH(CH3)2 SO2CH3 NMe2
1k-3: CH2CH(CH3)2 (C=O)CH3 NMe2

FIG. 36

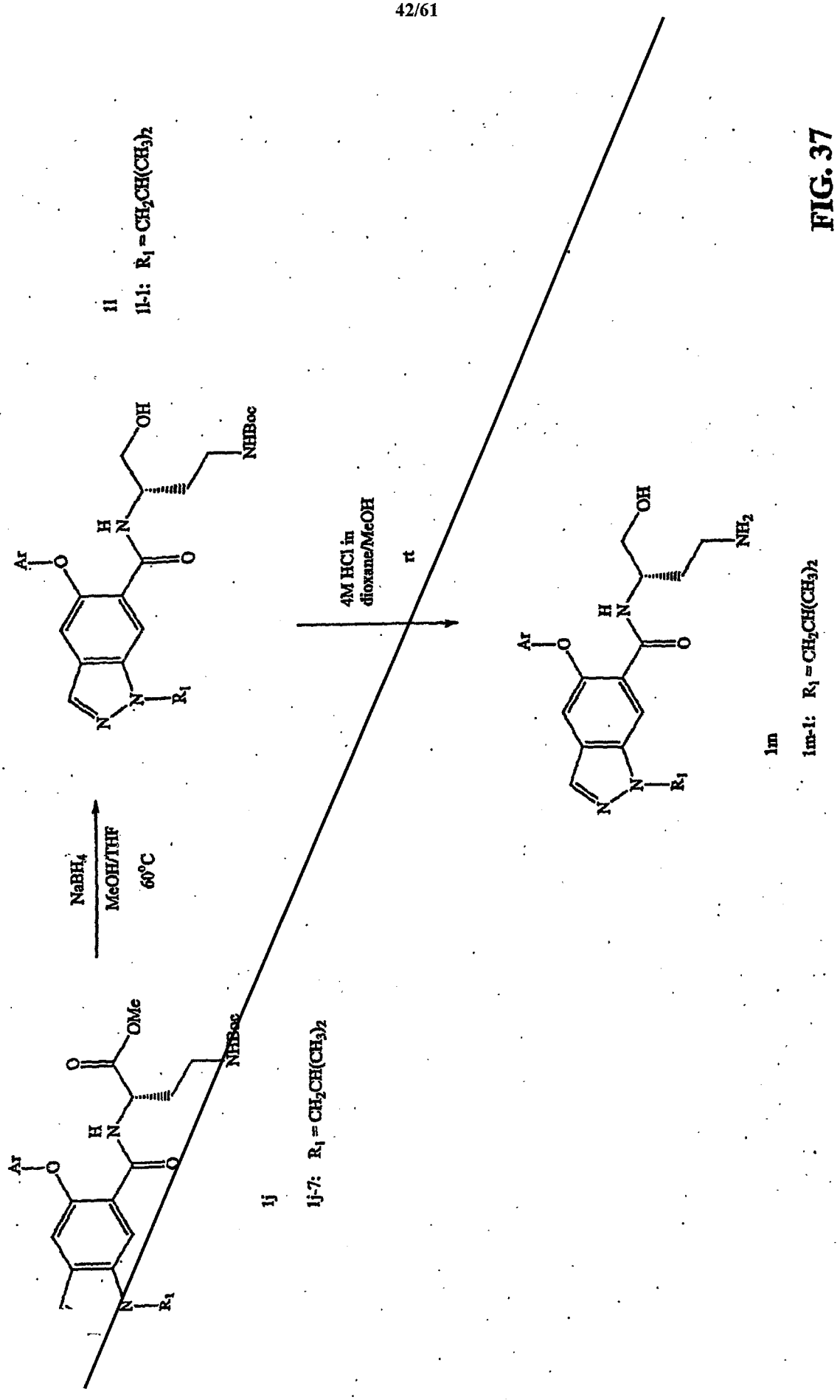

NaBH4
MeOH/THF
60°C
4M HCl in dioxane/MeOH
rt
1j
1j-7: R1 = CH2CH(CH3)2
1l
1l-1: R1 = CH2CH(CH3)2
1m
1m-1: R1 = CH2CH(CH3)2

FIG. 37

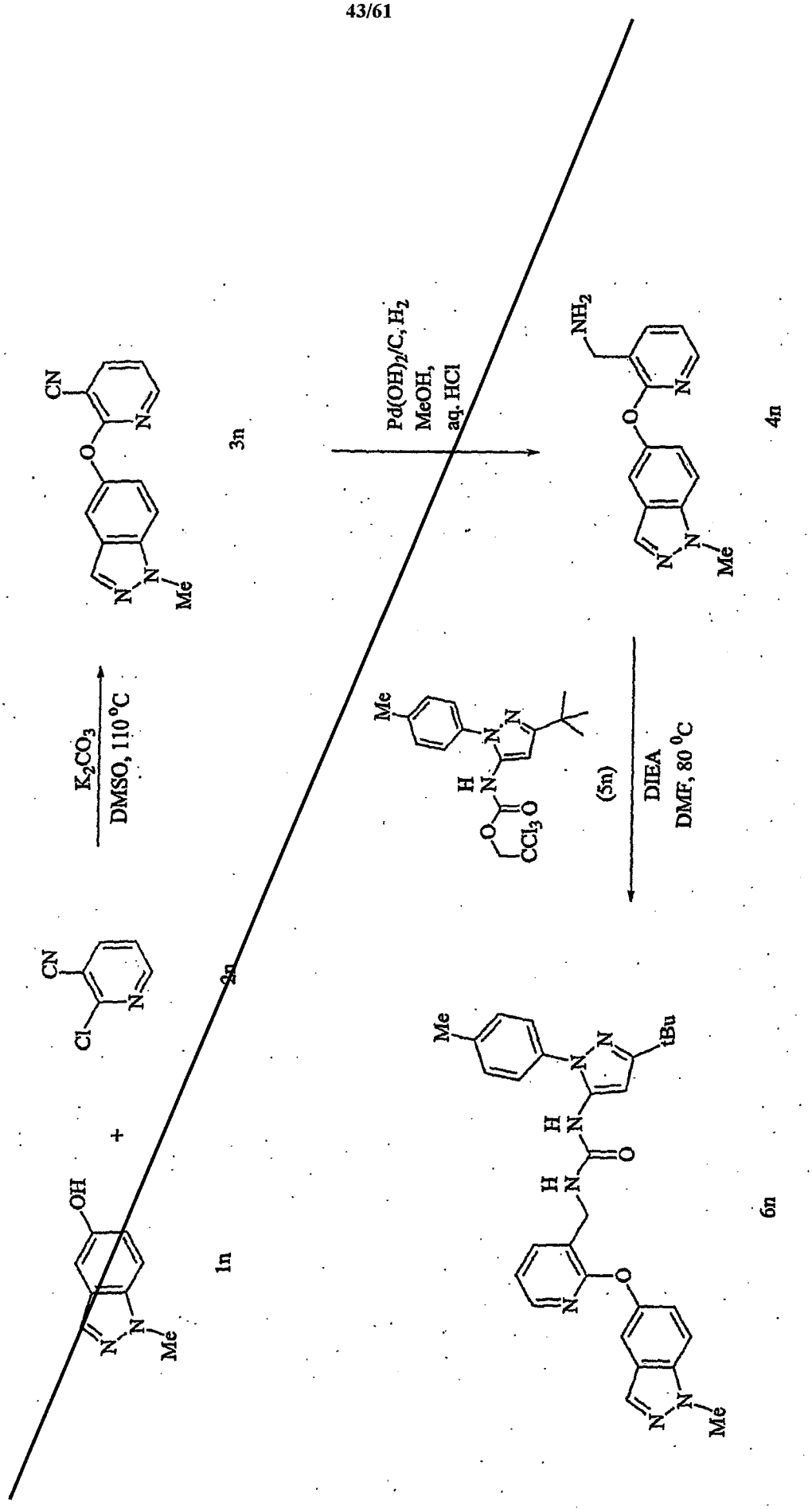

K2CO3
DMSO, 110 °C
Pd(OH)2/C, H2
MeOH,
aq. HCl
(5n)
DIEA
DMF, 80 °C
1n
2n
3n
4n
6n

FIG. 38

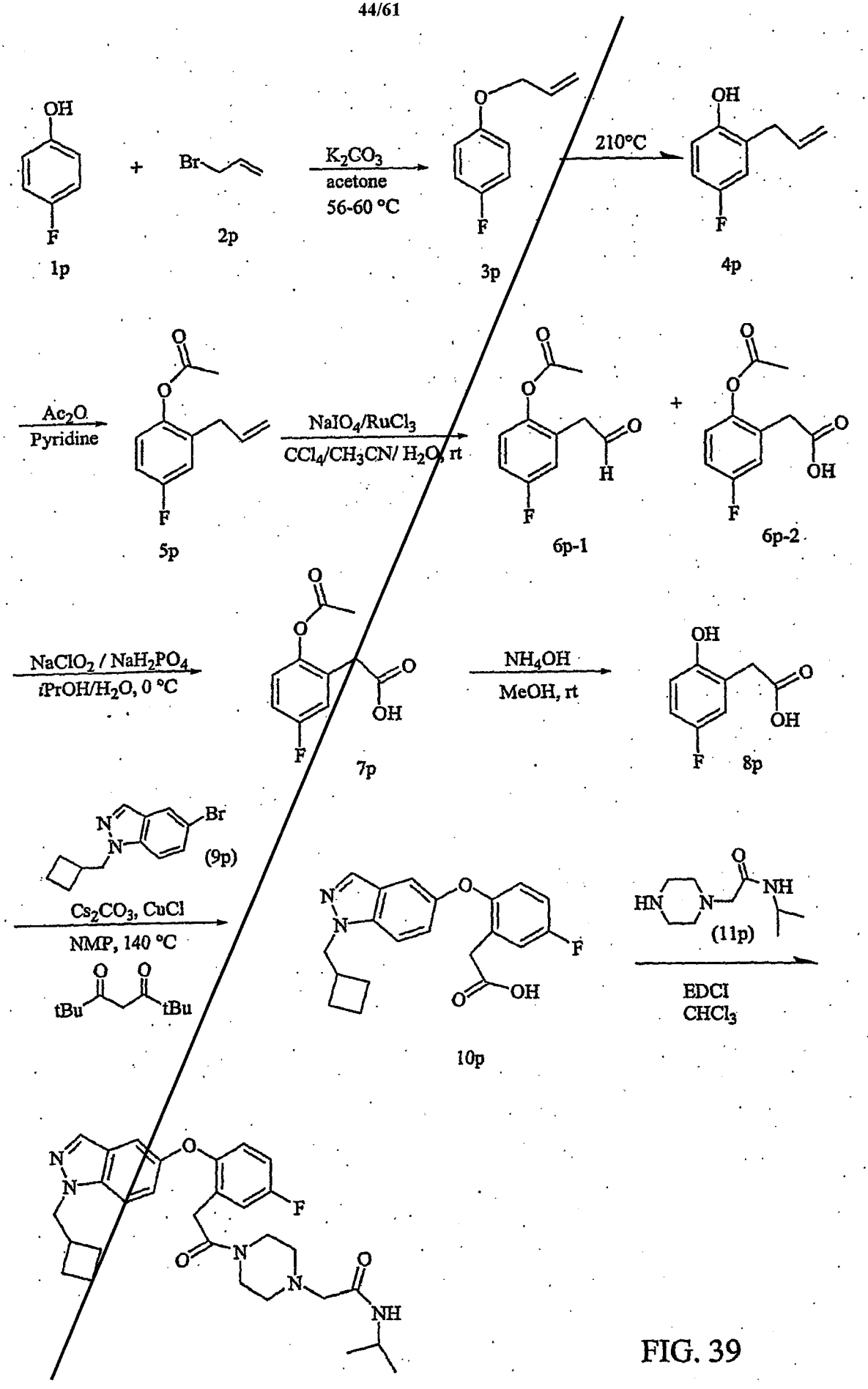

OH
F
1p
Br
2p
K_2CO_3
acetone
56-60 °C
3p
210°C
4p
Ac_2O
Pyridine
5p
$NaIO_4/RuCl_3$
$CCl_4/CH_3CN/H_2O$, rt
6p-1
6p-2
$NaClO_2$ / NaH_2PO_4
$iPrOH/H_2O$, 0 °C
7p
NH_4OH
MeOH, rt
8p
(9p)
Cs_2CO_3, CuCl
NMP, 140 °C
tBu
tBu
10p
(11p)
EDCI
$CHCl_3$

FIG. 39

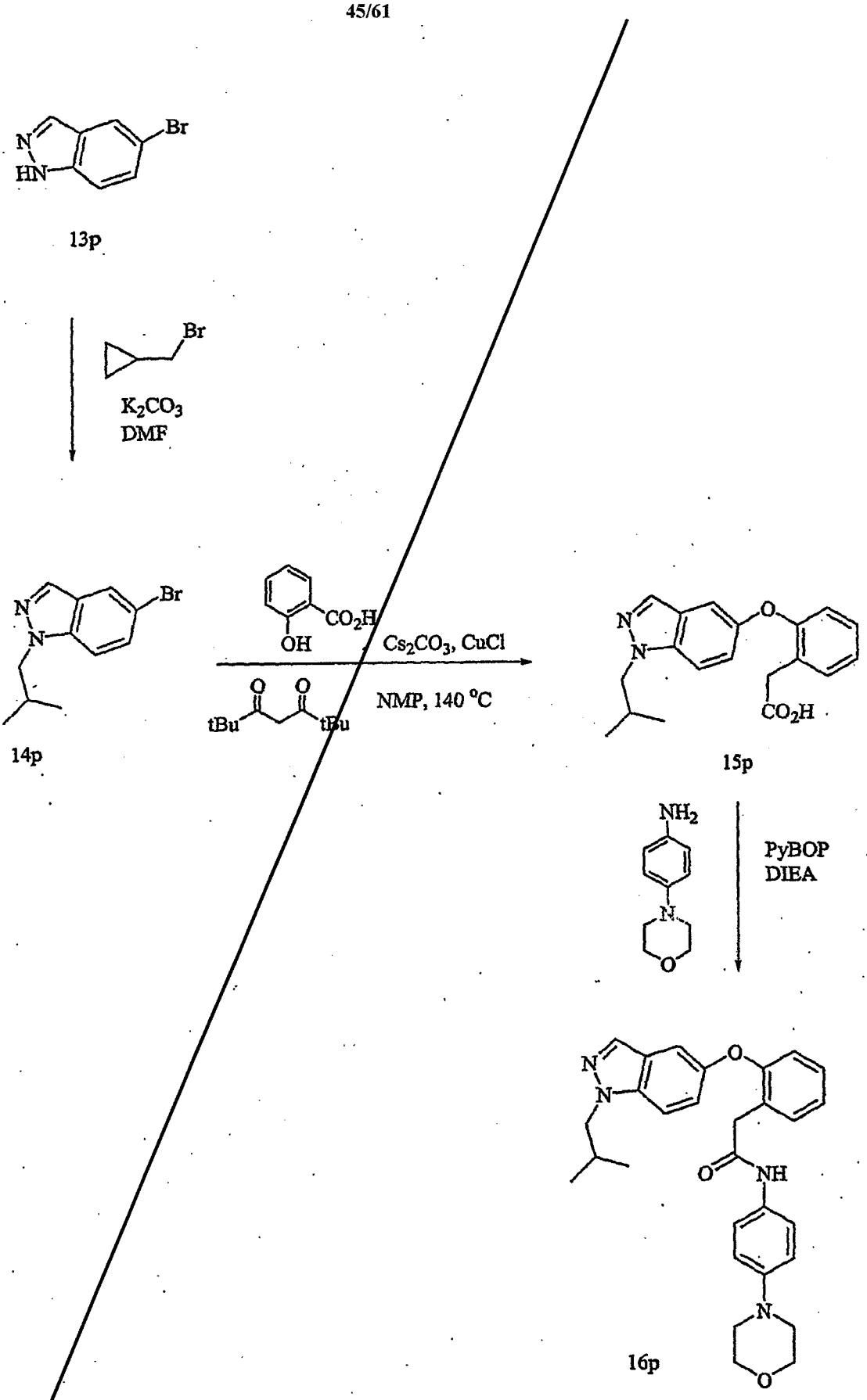

Br
N
HN
13p
Br
K_2CO_3
DMF
Br
N
N
14p
CO_2H
OH
Cs_2CO_3, CuCl
NMP, 140 °C
tBu
tBu
O
O
O
N
N
O
CO_2H
15p
NH_2
N
O
PyBOP
DIEA
O
N
N
O
NH
N
O
16p

FIG. 40

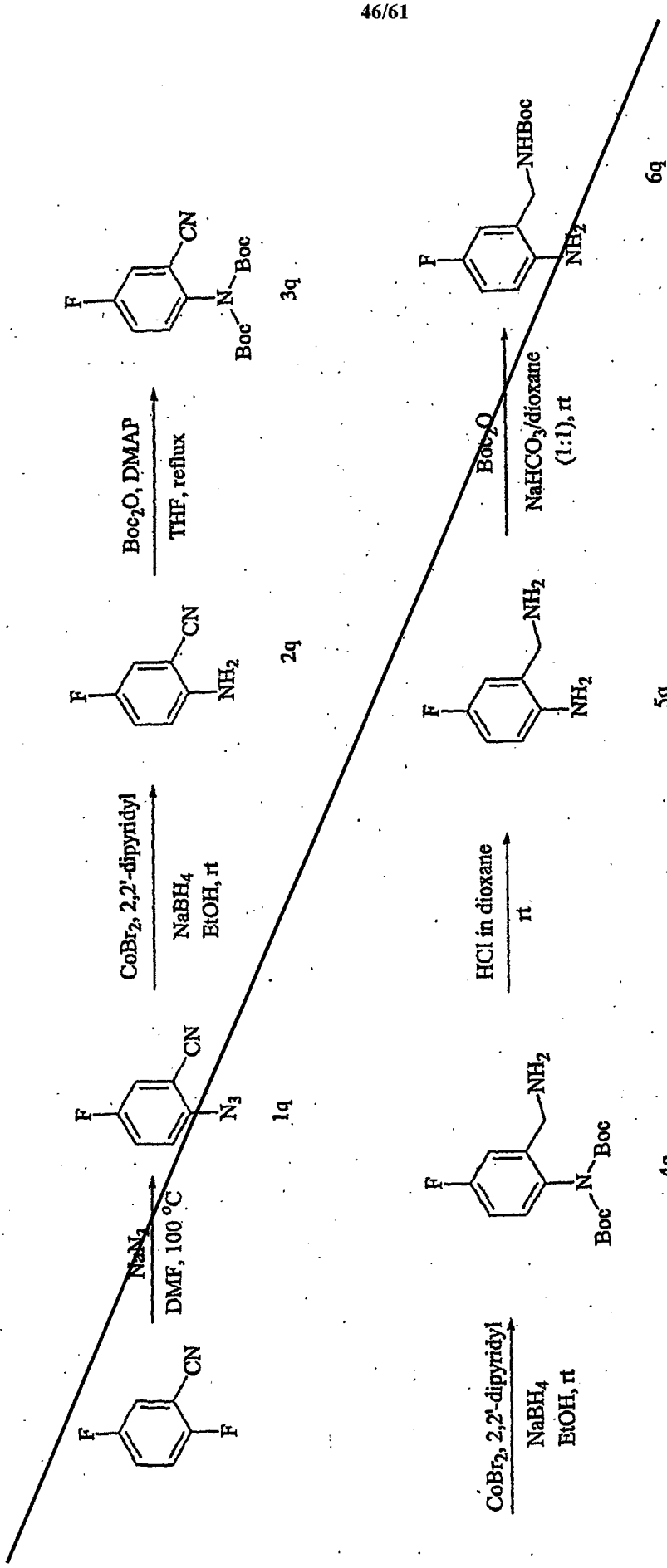

NaN3
DMF, 100 °C
CoBr2, 2,2'-dipyridyl
NaBH4
EtOH, rt
Boc2O, DMAP
THF, reflux
HCl in dioxane
rt
Boc2O
NaHCO3/dioxane
(1:1), rt
CoBr2, 2,2'-dipyridyl
NaBH4
EtOH, rt
1q
2q
3q
4q
5q
6q

FIG. 41A

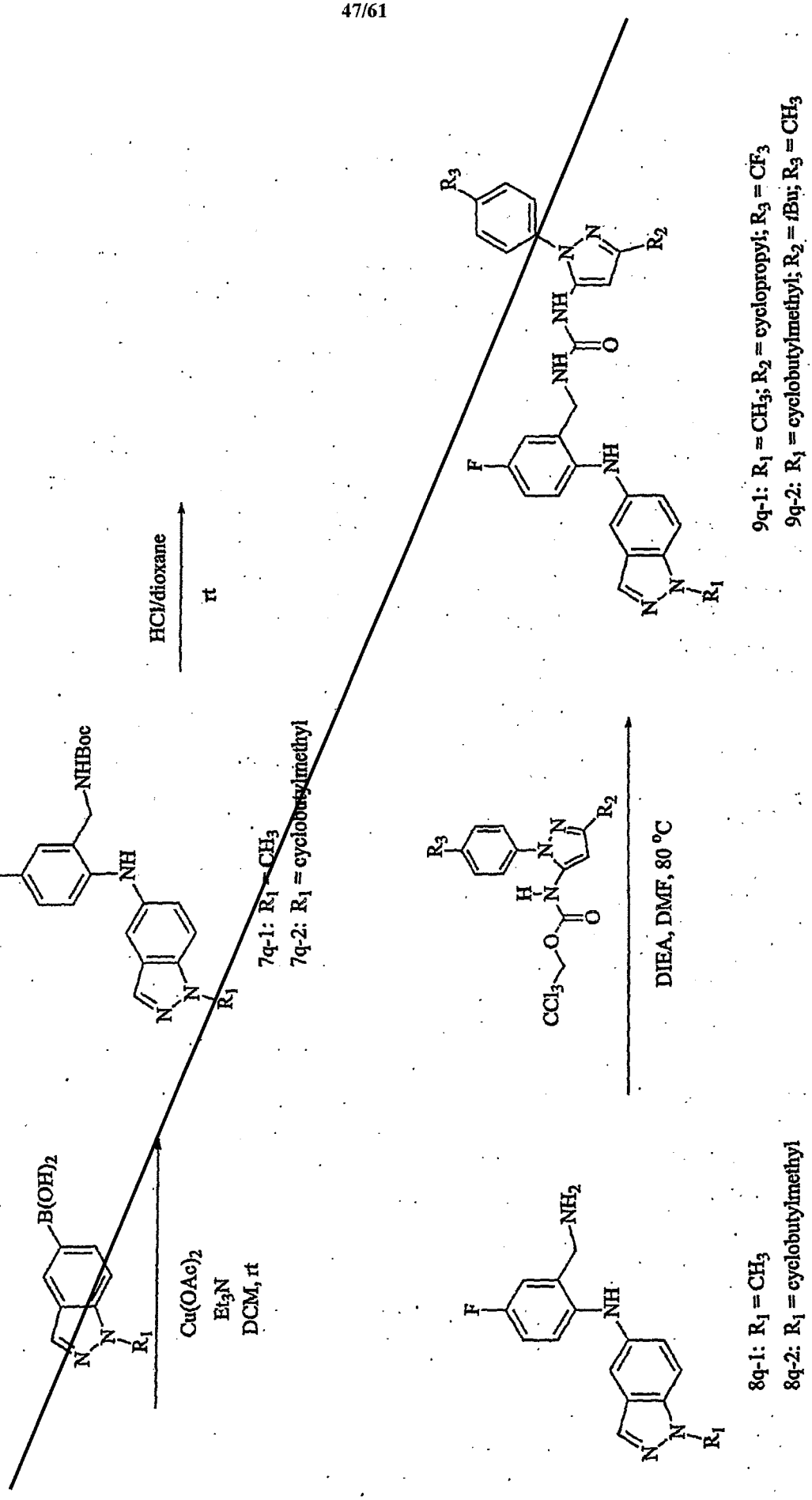
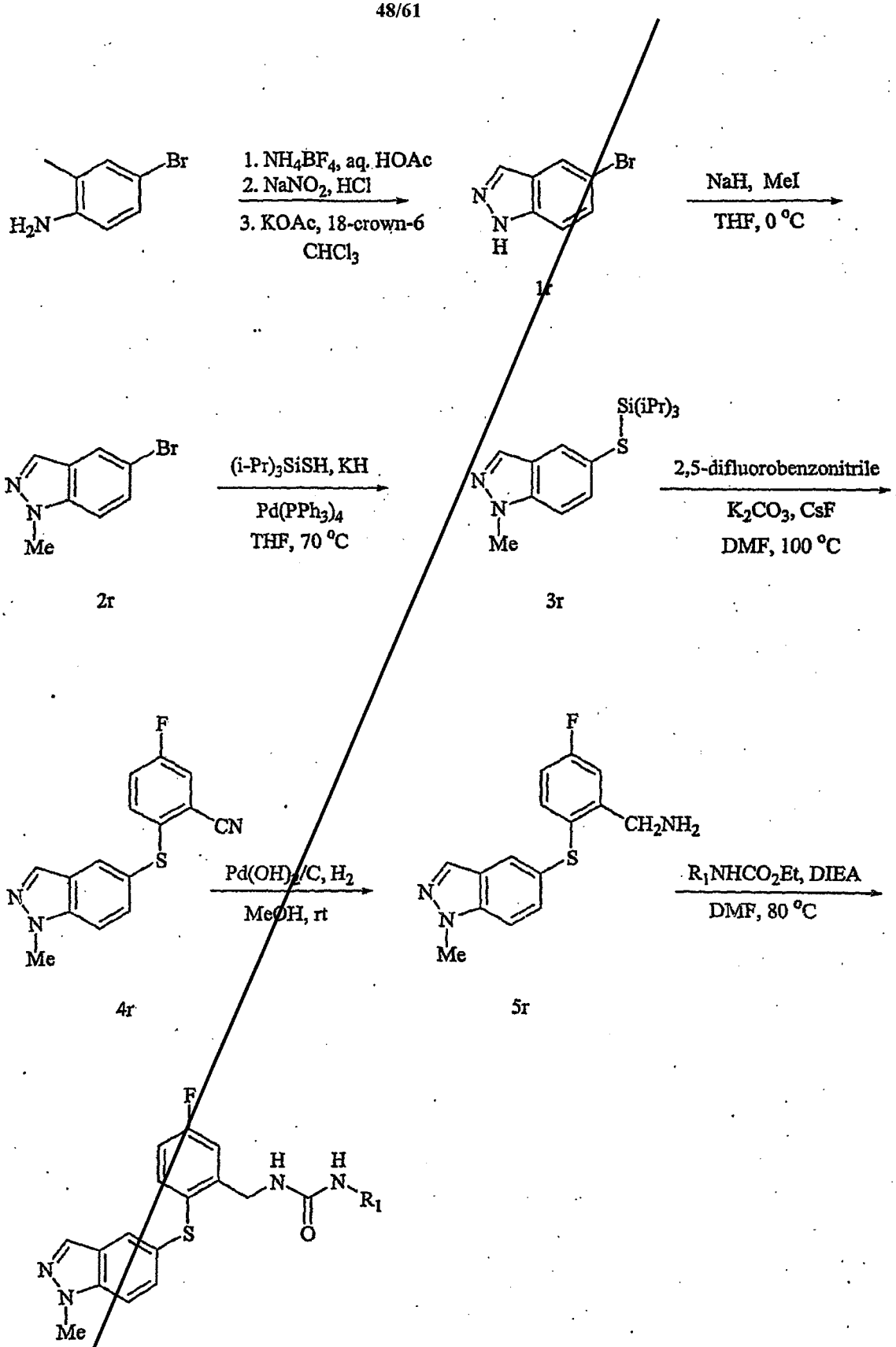

B(OH)2
Cu(OAc)2
Et3N
DCM, rt
NHBoc
HCl/dioxane
rt
7q-1: R1 = CH3
7q-2: R1 = cyclobutylmethyl
NH2
DIEA, DMF, 80 °C
CCl3
8q-1: R1 = CH3
8q-2: R1 = cyclobutylmethyl
9q-1: R1 = CH3; R2 = cyclopropyl; R3 = CF3
9q-2: R1 = cyclobutylmethyl; R2 = tBu; R3 = CH3

FIG. 41B



1r 2r 3r 4r 5r

6r-1: R_1 = 5-cyclopropyl-2-(4'-chlorophenyl)-2H-pyrazol-3-yl

4'-chlorophenyl)-2H-pyrazol-3-yl

FIG. 42

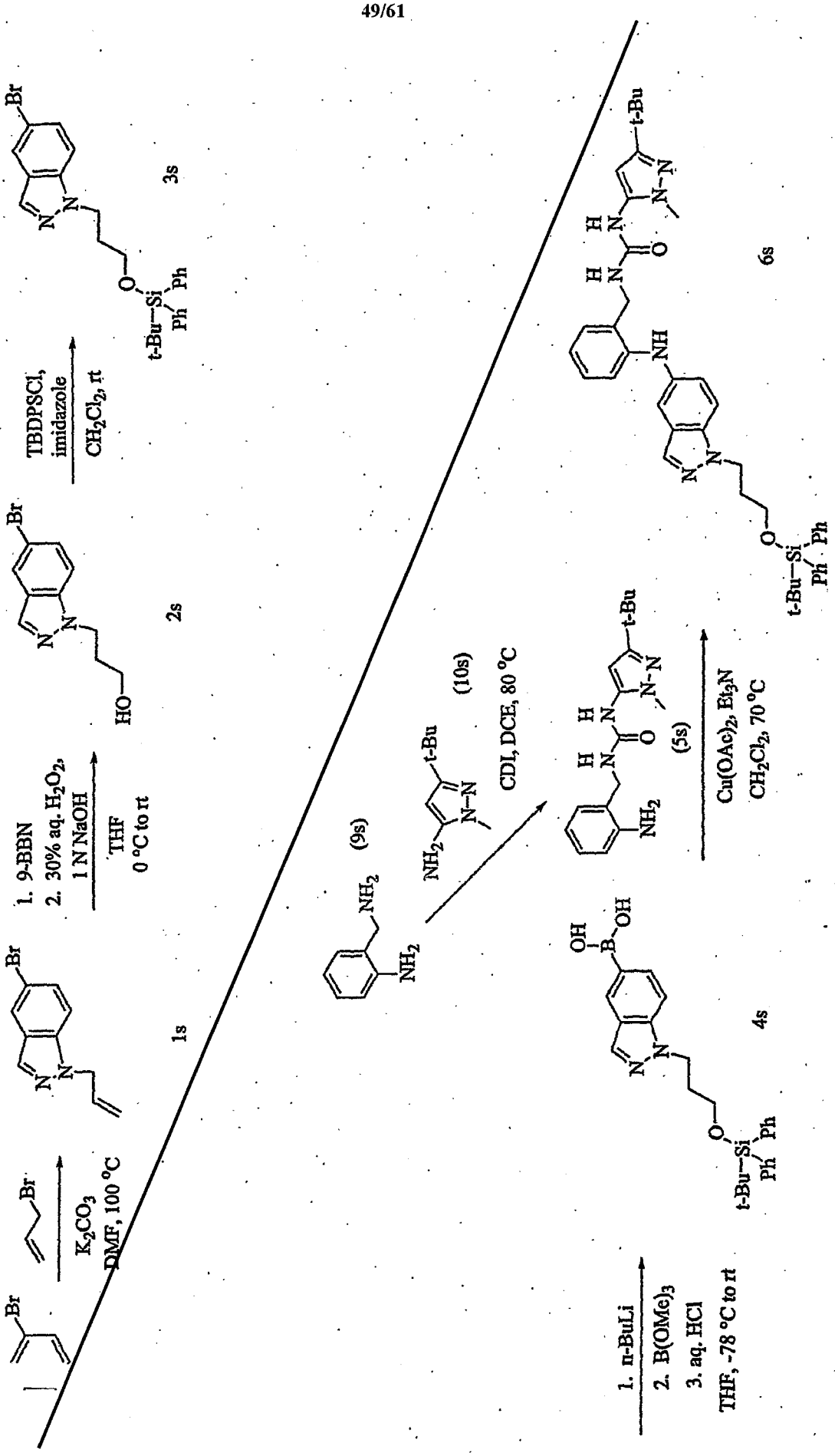

1. 9-BBN
2. 30% aq. H2O2, 1 N NaOH
THF
0 °C to rt
TBDPSCl, imidazole
CH2Cl2, rt
K2CO3
DMF, 100 °C
1. n-BuLi
2. B(OMe)3
3. aq. HCl
THF, -78 °C to rt
CDI, DCE, 80 °C
Cu(OAc)2, Et3N
CH2Cl2, 70 °C
1s
2s
3s
4s
(5s)
(9s)
(10s)
6s

FIG. 43A

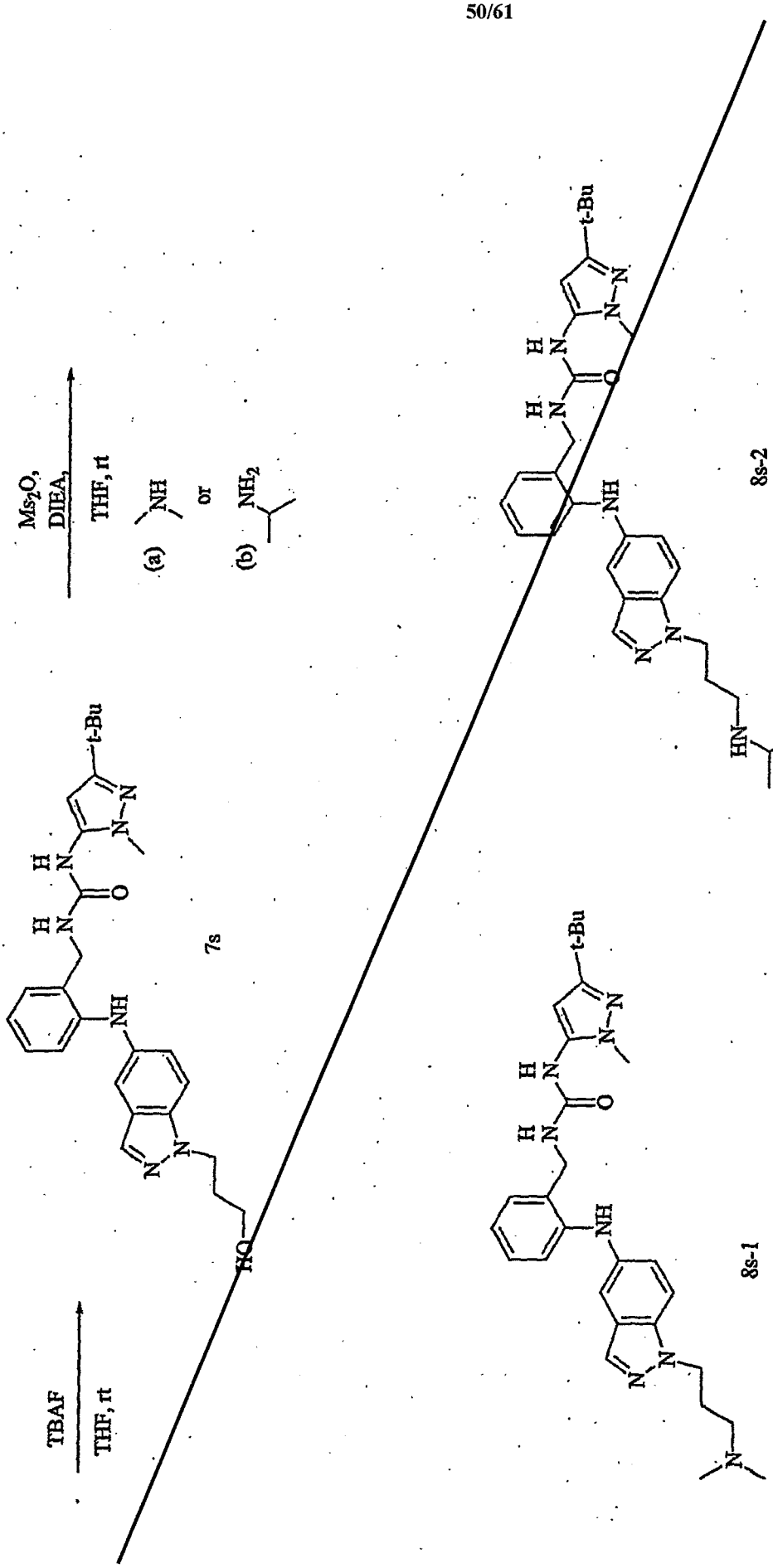


FIG. 43B

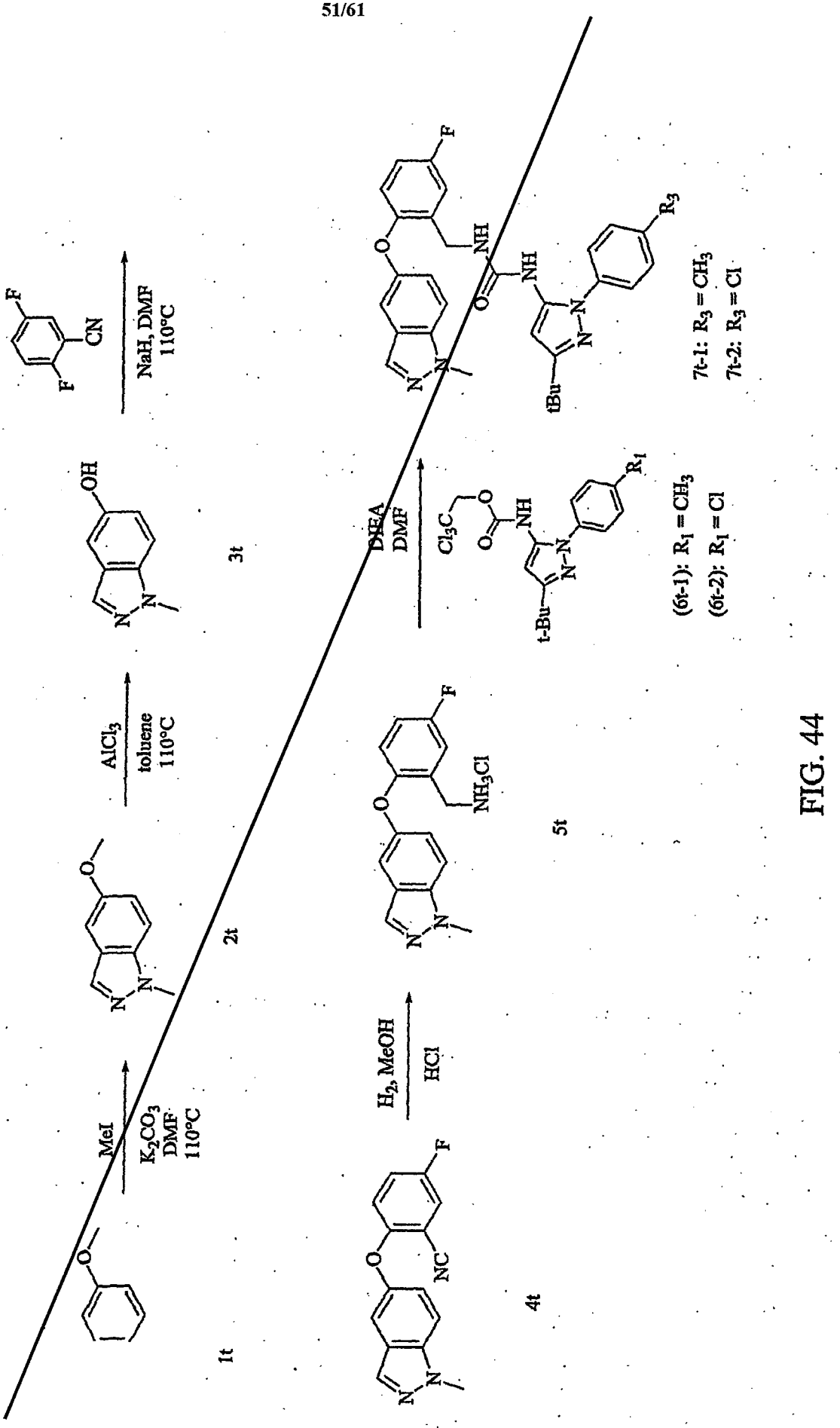

MeI
K_2CO_3
DMF
110°C
1t
2t
$AlCl_3$
toluene
110°C
3t
NaH, DMF
110°C
H_2, MeOH
HCl
4t
5t
DIEA
DMF
(6t-1): $R_1 = CH_3$
(6t-2): $R_1 = Cl$
7t-1: $R_3 = CH_3$
7t-2: $R_3 = Cl$

FIG. 44

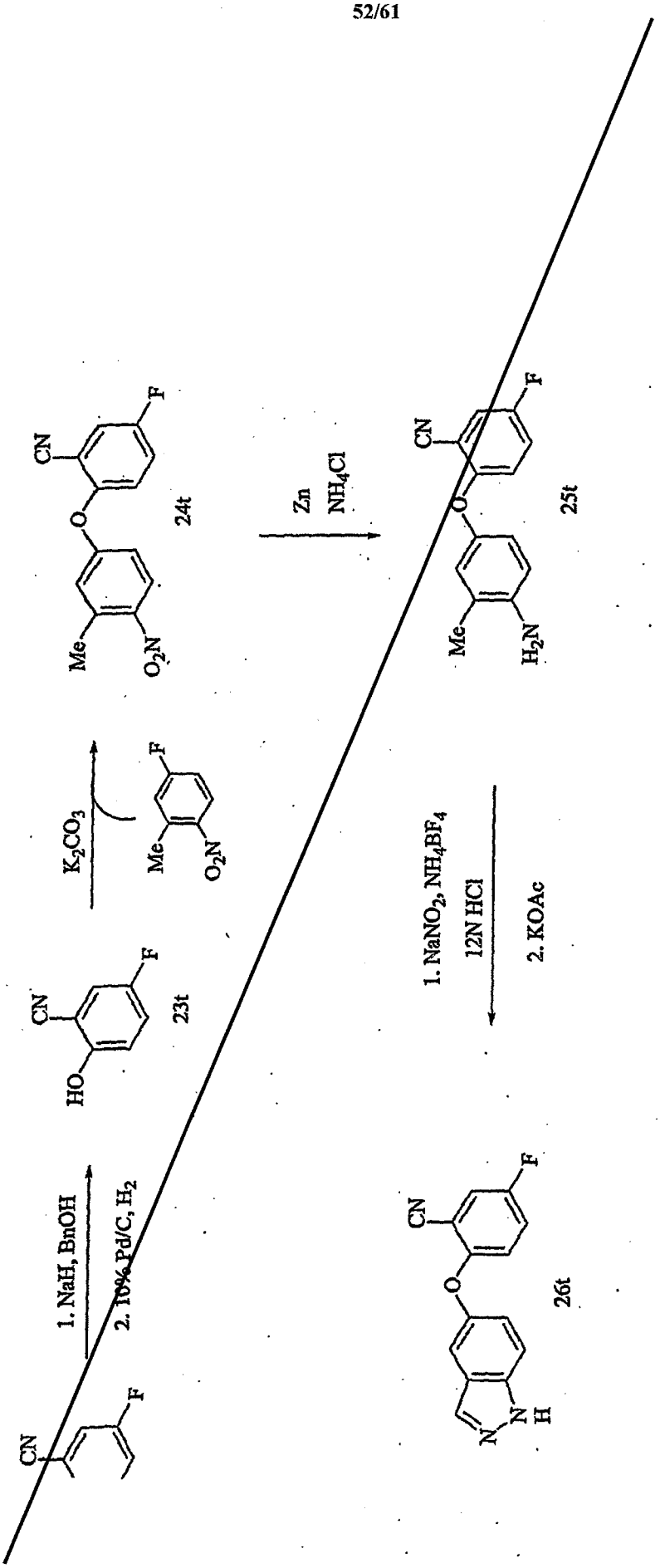

1. NaH, BnOH
2. 10% Pd/C, H2
23t
K2CO3
24t
Zn
NH4Cl
25t
1. NaNO2, NH4BF4
12N HCl
2. KOAc
26t

FIG. 45

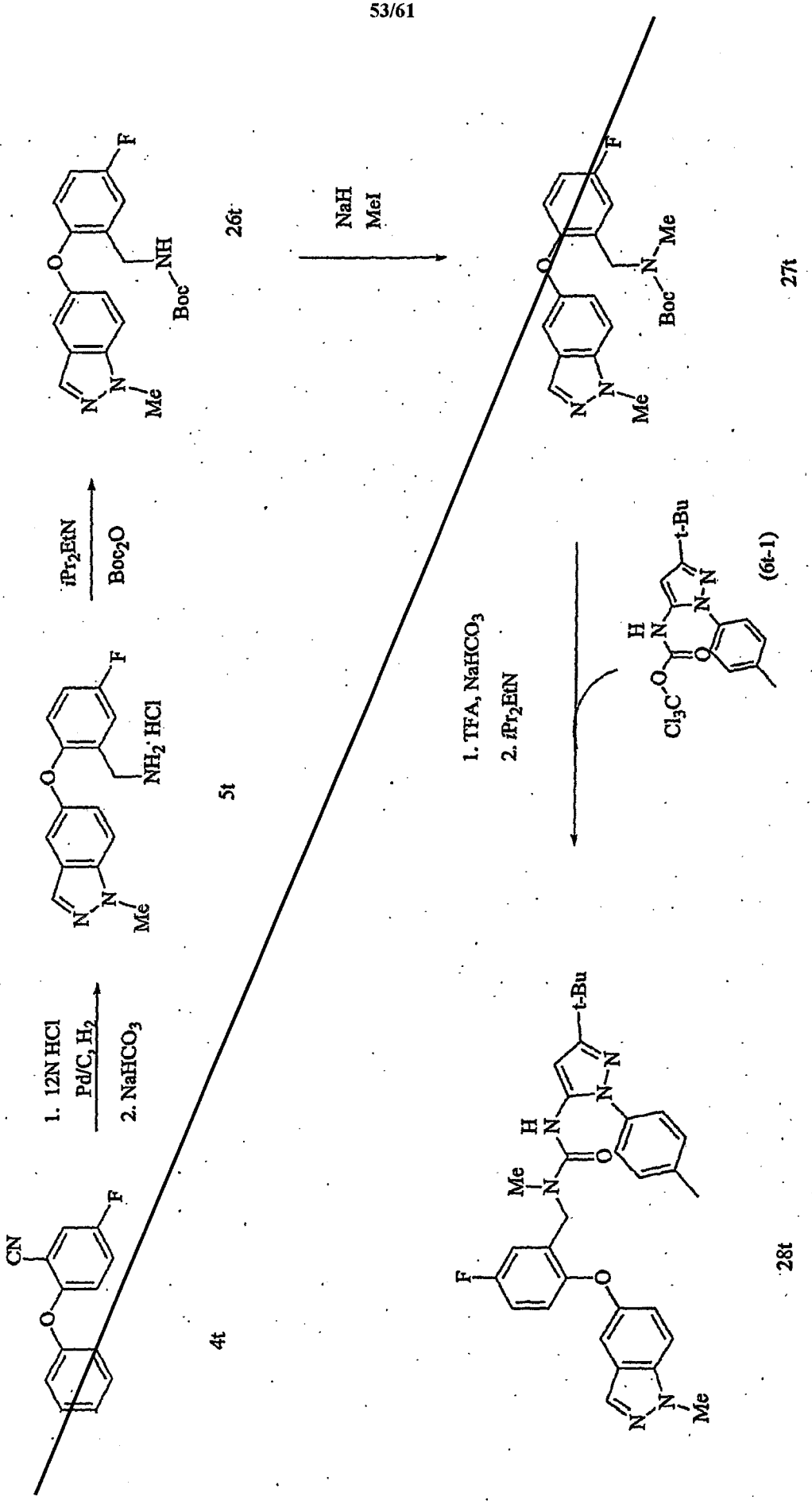

1. 12N HCl
Pd/C, H2
2. NaHCO3
iPr2EtN
Boc2O
NaH
MeI
1. TFA, NaHCO3
2. iPr2EtN
4t
5t
26t
27t
28t
(6t-1)
F
CN
O
NH2 · HCl
NH
Boc
N
Me
t-Bu
H
Cl3C

FIG. 46

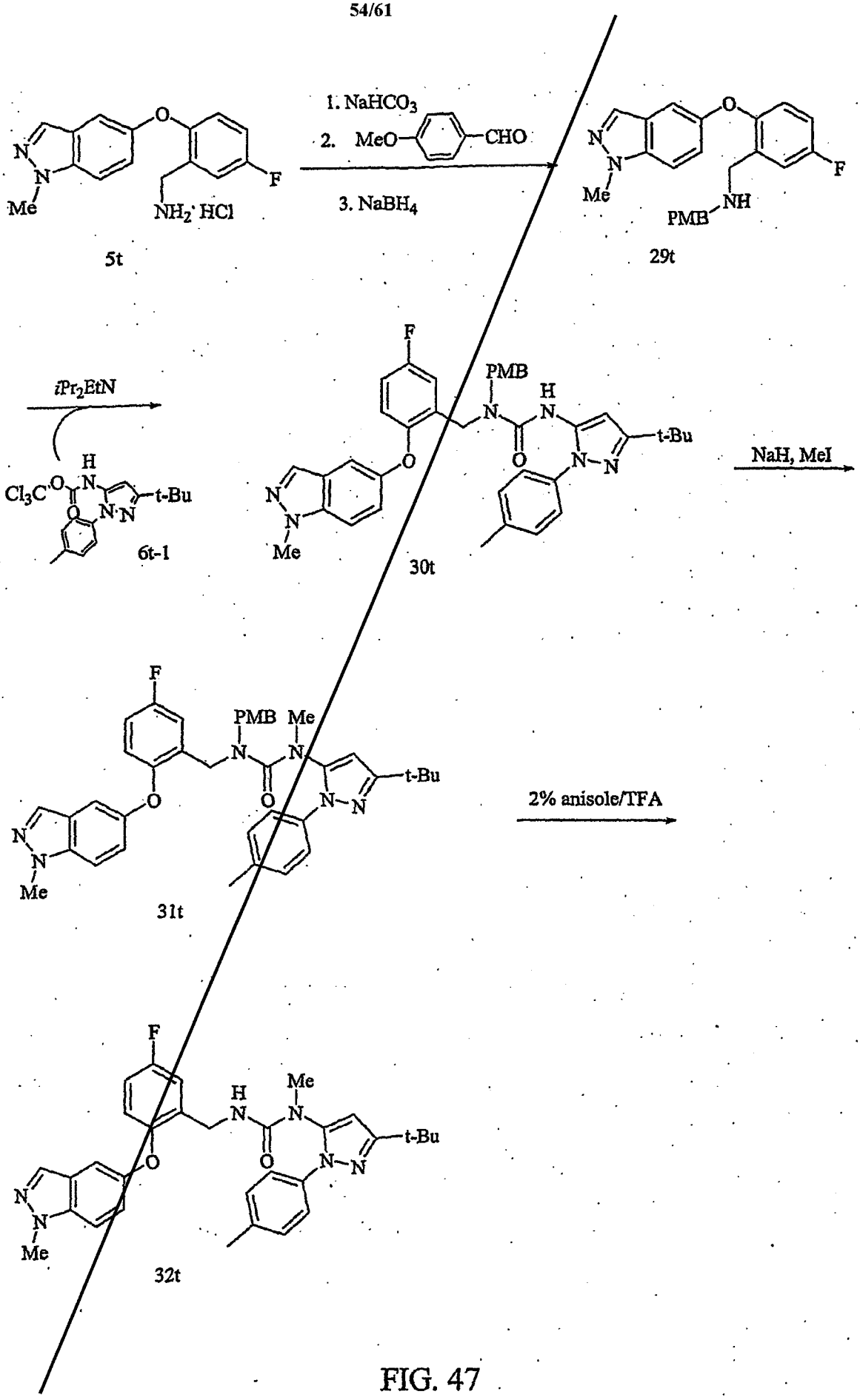

1. NaHCO3
2. MeO
CHO
3. NaBH4
Me
NH2 HCl
F
5t
29t
PMB
NH
iPr2EtN
Cl3C
t-Bu
6t-1
30t
NaH, MeI
31t
2% anisole/TFA
32t

FIG. 47

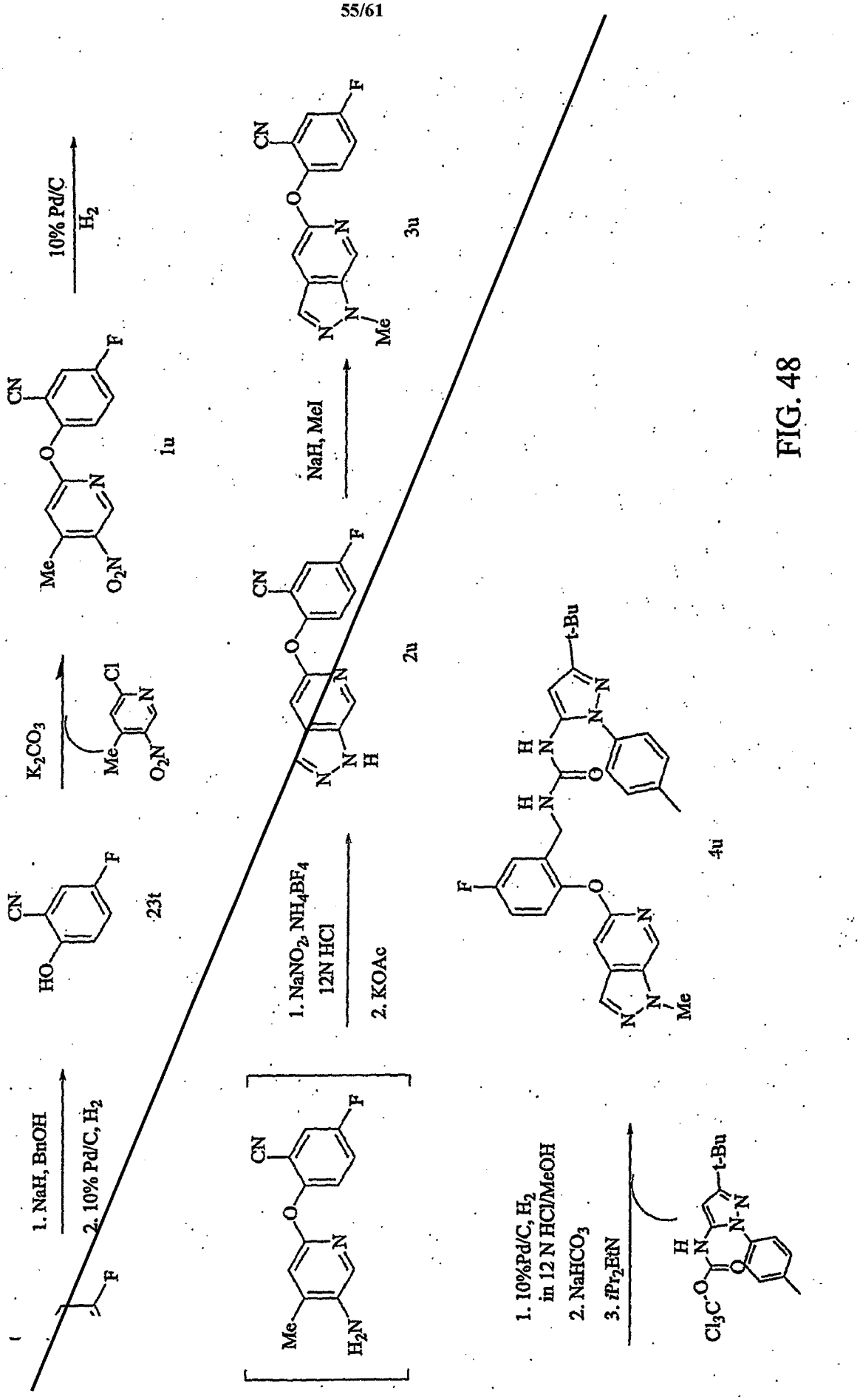

1. NaH, BnOH
2. 10% Pd/C, H2
23t
K2CO3
1u
10% Pd/C
H2
1. NaNO2, NH4BF4
12N HCl
2. KOAc
2u
NaH, MeI
3u
1. 10%Pd/C, H2
in 12 N HCl/MeOH
2. NaHCO3
3. iPr2EtN
4u

FIG. 48

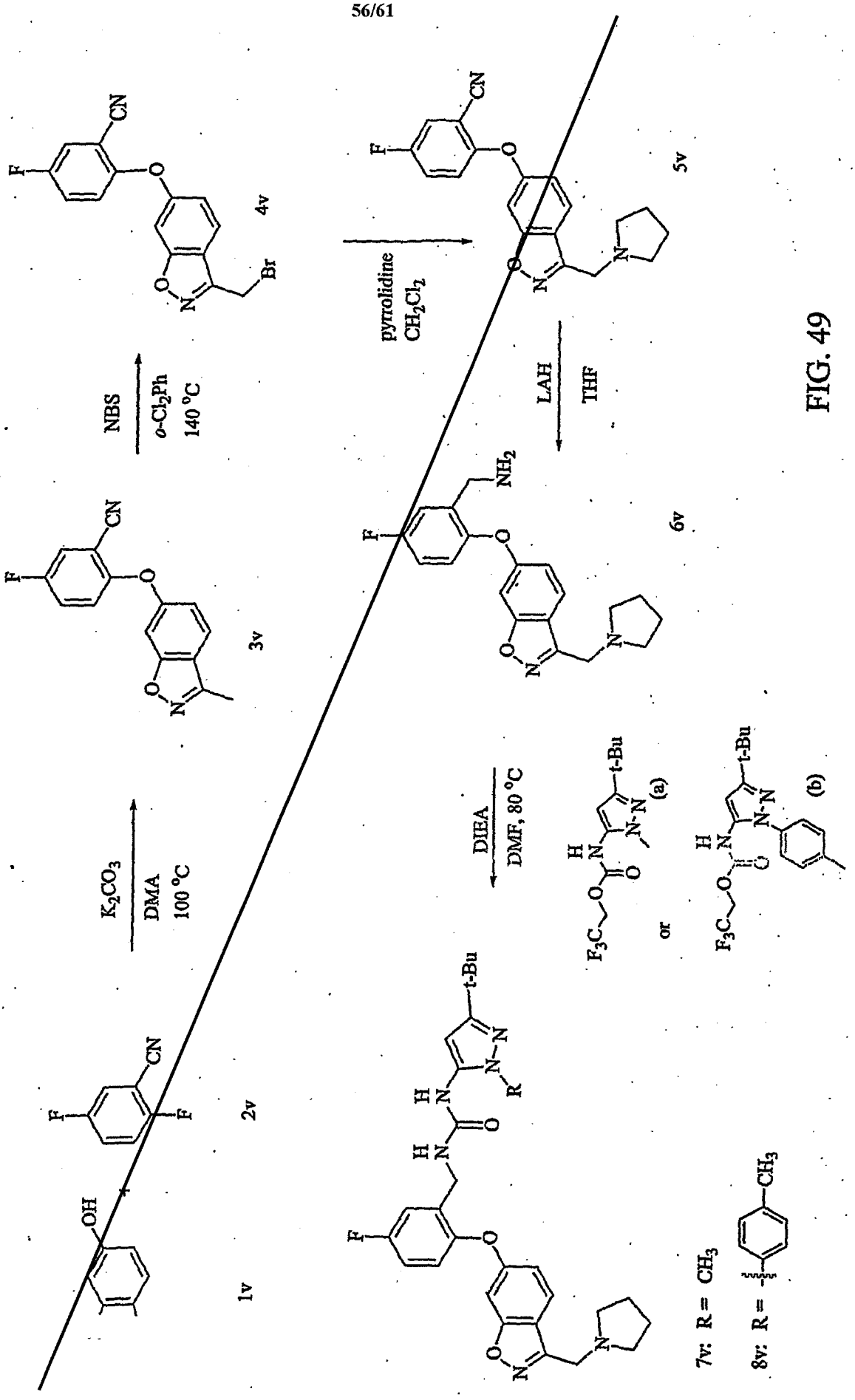

1v
2v
3v
4v
5v
6v
7v: R = CH3
8v: R =
K2CO3
DMA
100 °C
NBS
o-Cl2Ph
140 °C
pyrrolidine
CH2Cl2
LAH
THF
DIEA
DMF, 80 °C
or
(a)
(b)

FIG. 49

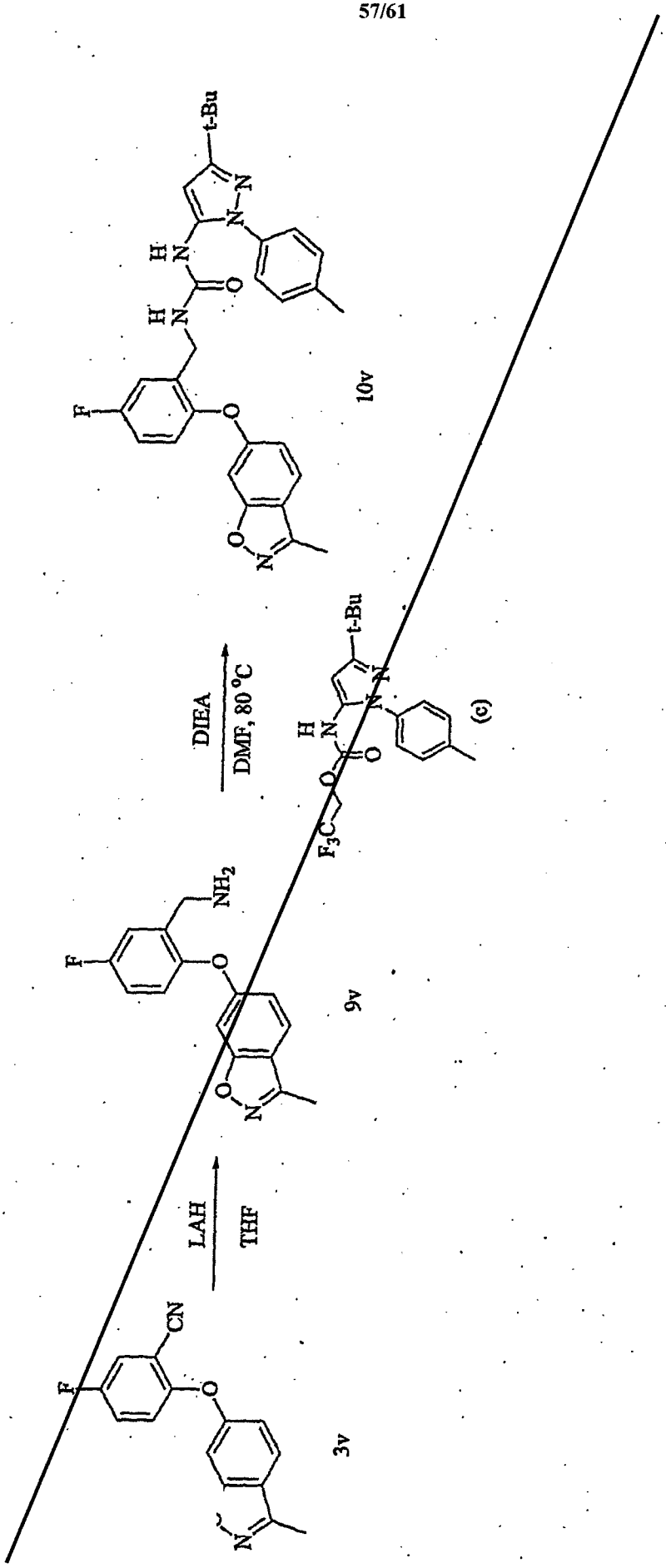


FIG. 50

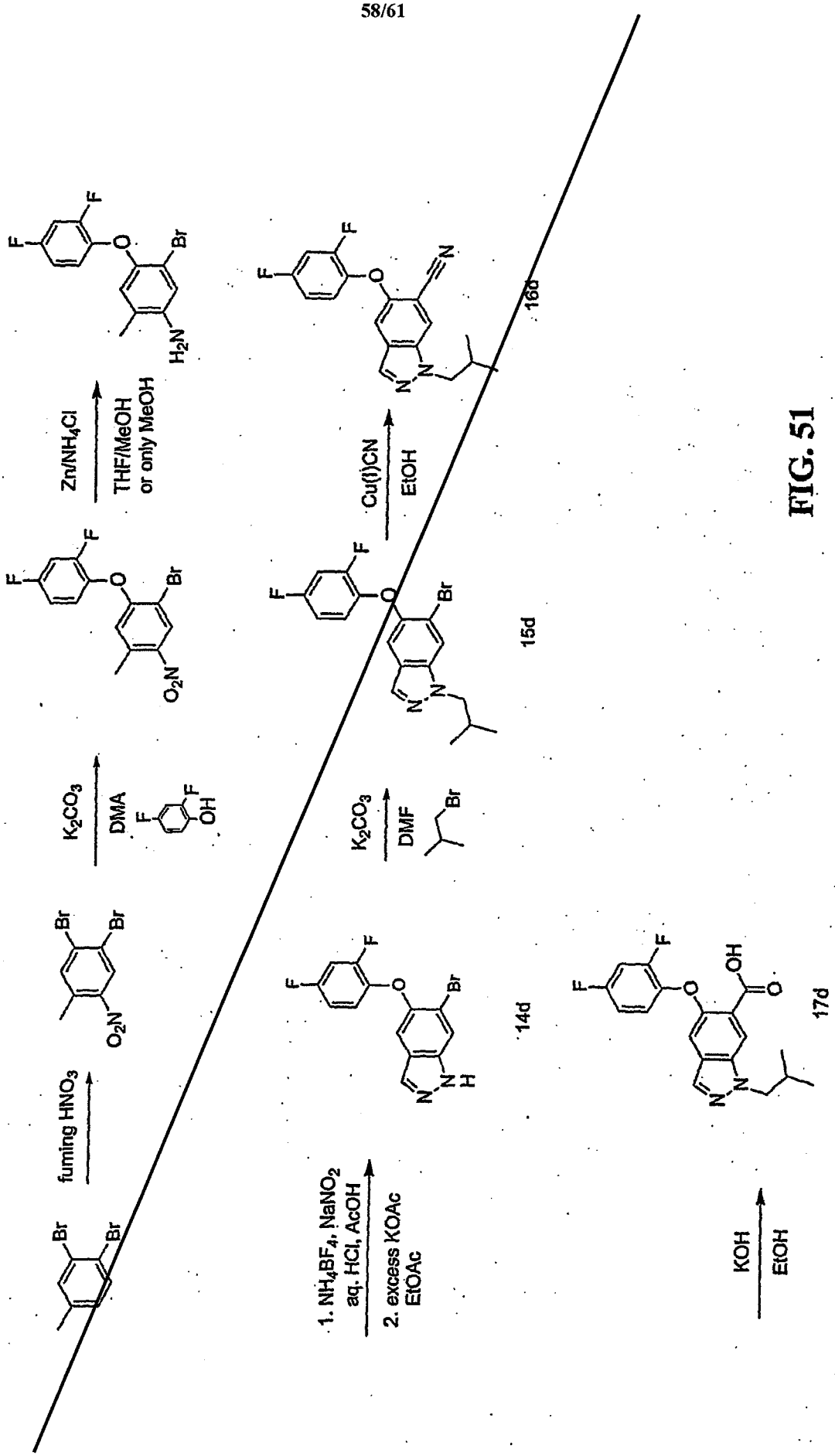

fuming HNO3
K2CO3
DMA
Zn/NH4Cl
THF/MeOH
or only MeOH
1. NH4BF4, NaNO2
aq. HCl, AcOH
2. excess KOAc
EtOAc
K2CO3
DMF
Cu(I)CN
EtOH
KOH
EtOH
14d
15d
16d
17d

FIG. 51

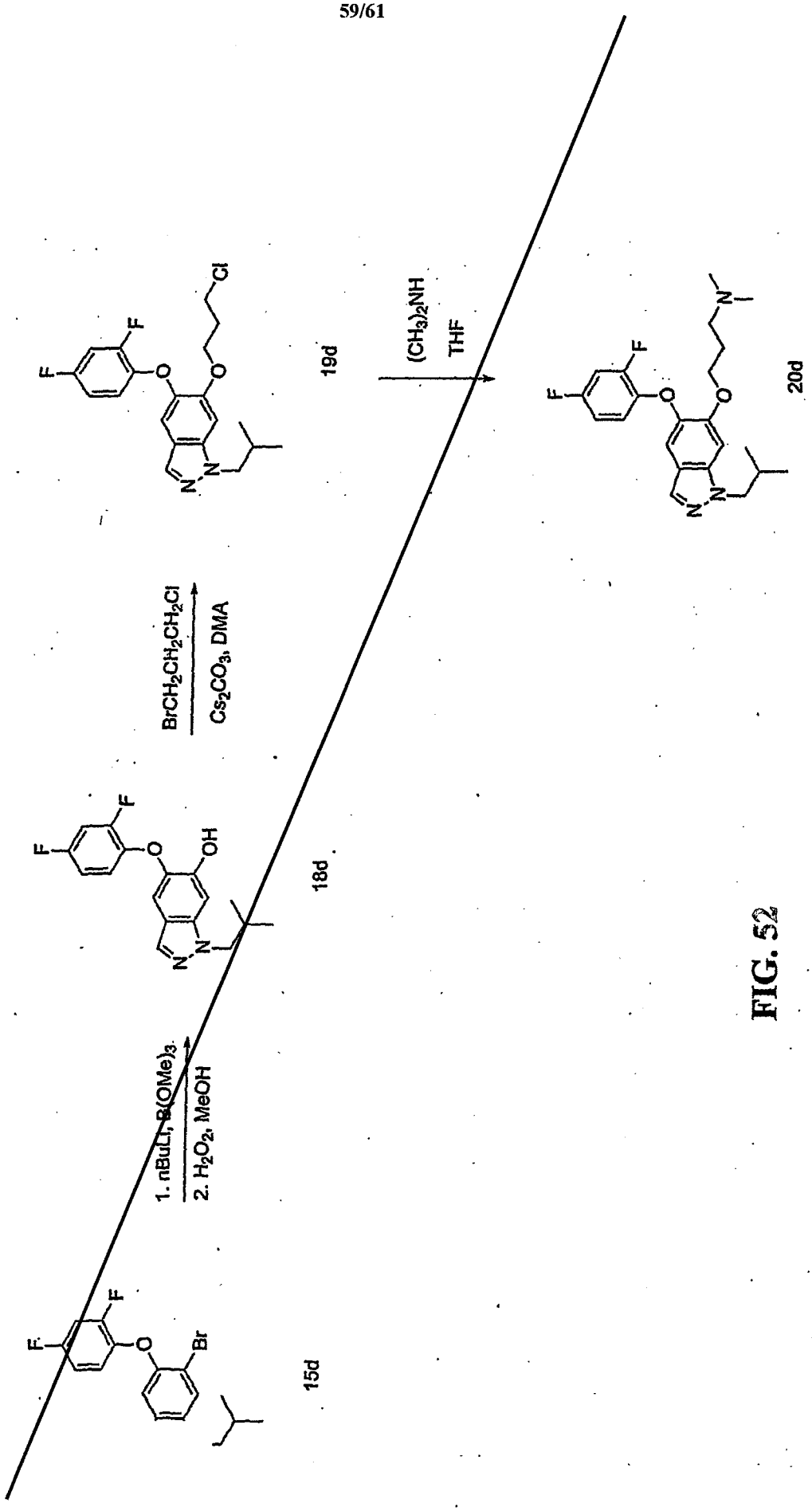

1. nBuLi, B(OMe)3
2. H2O2, MeOH
BrCH2CH2CH2Cl
Cs2CO3, DMA
(CH3)2NH
THF
15d
18d
19d
20d

FIG. 52

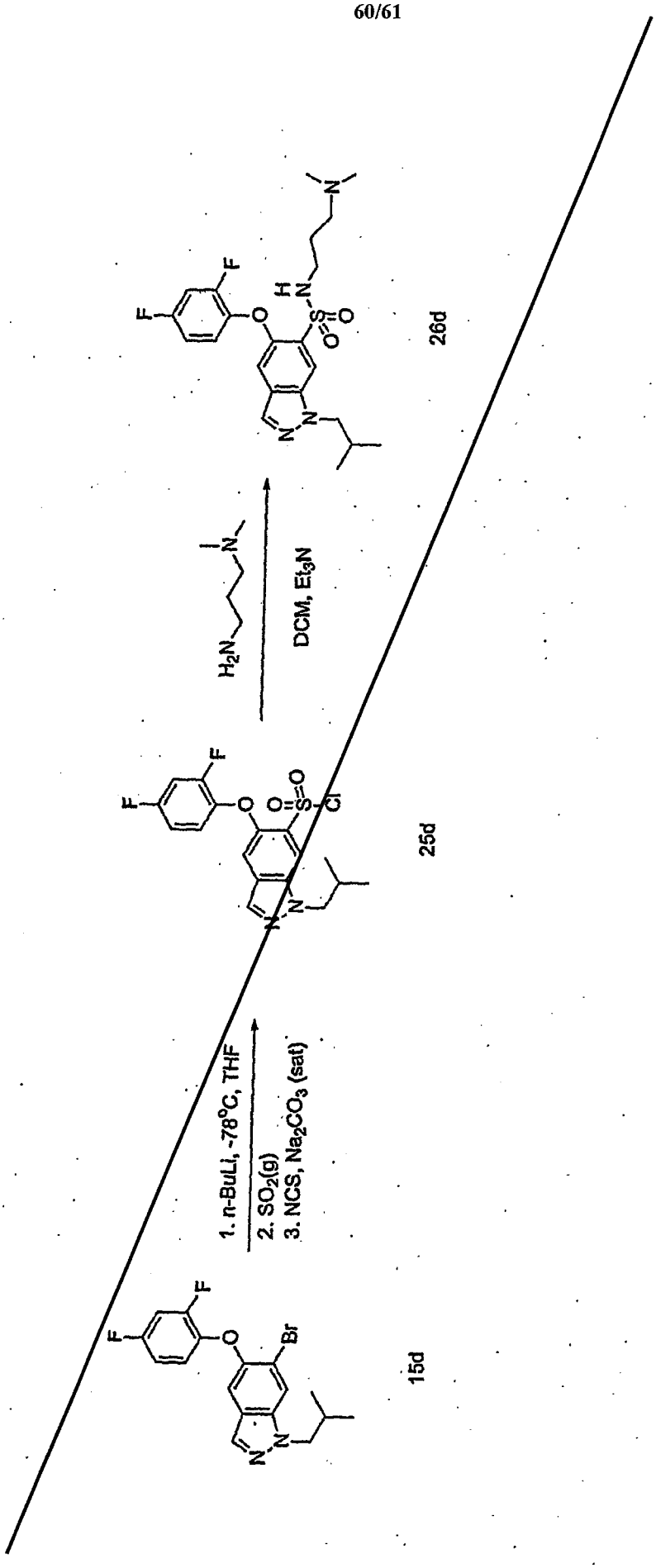


FIG. 53

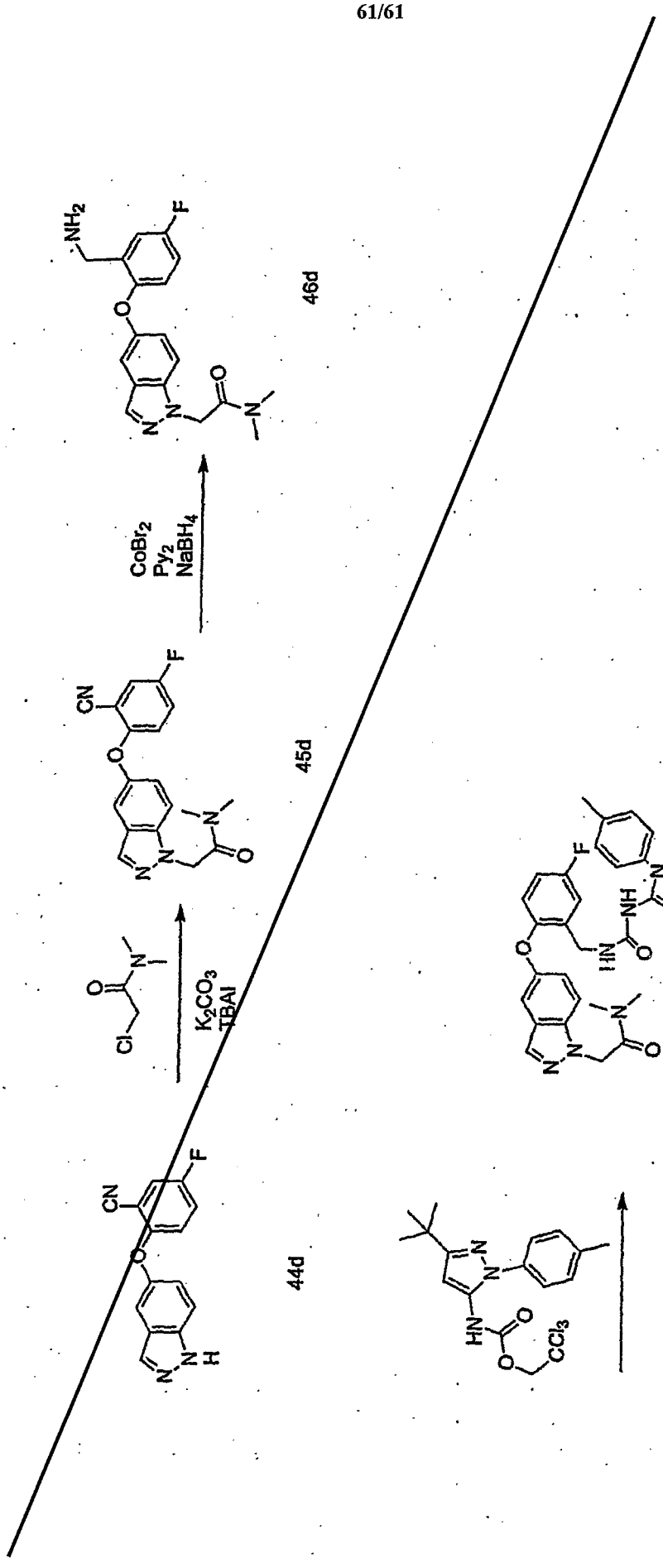
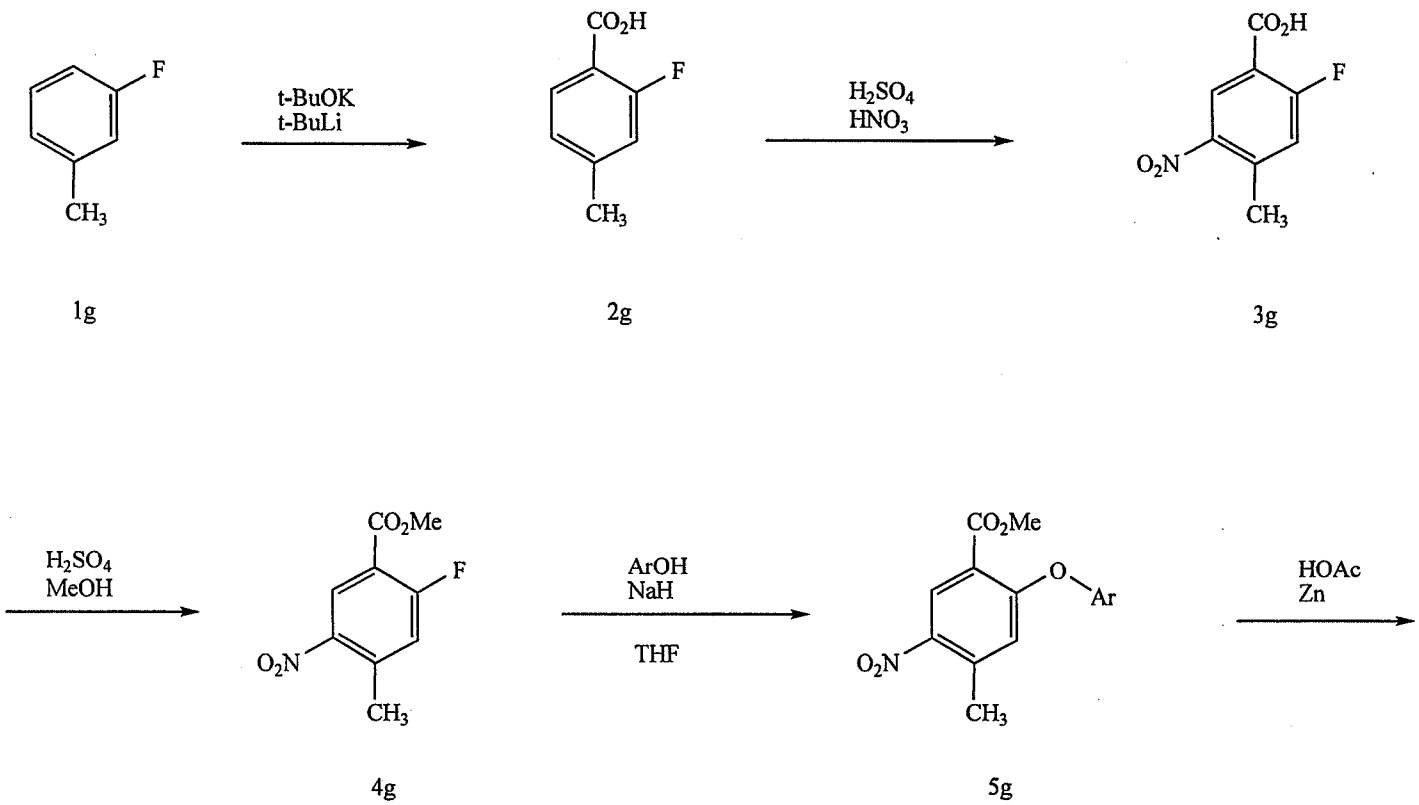


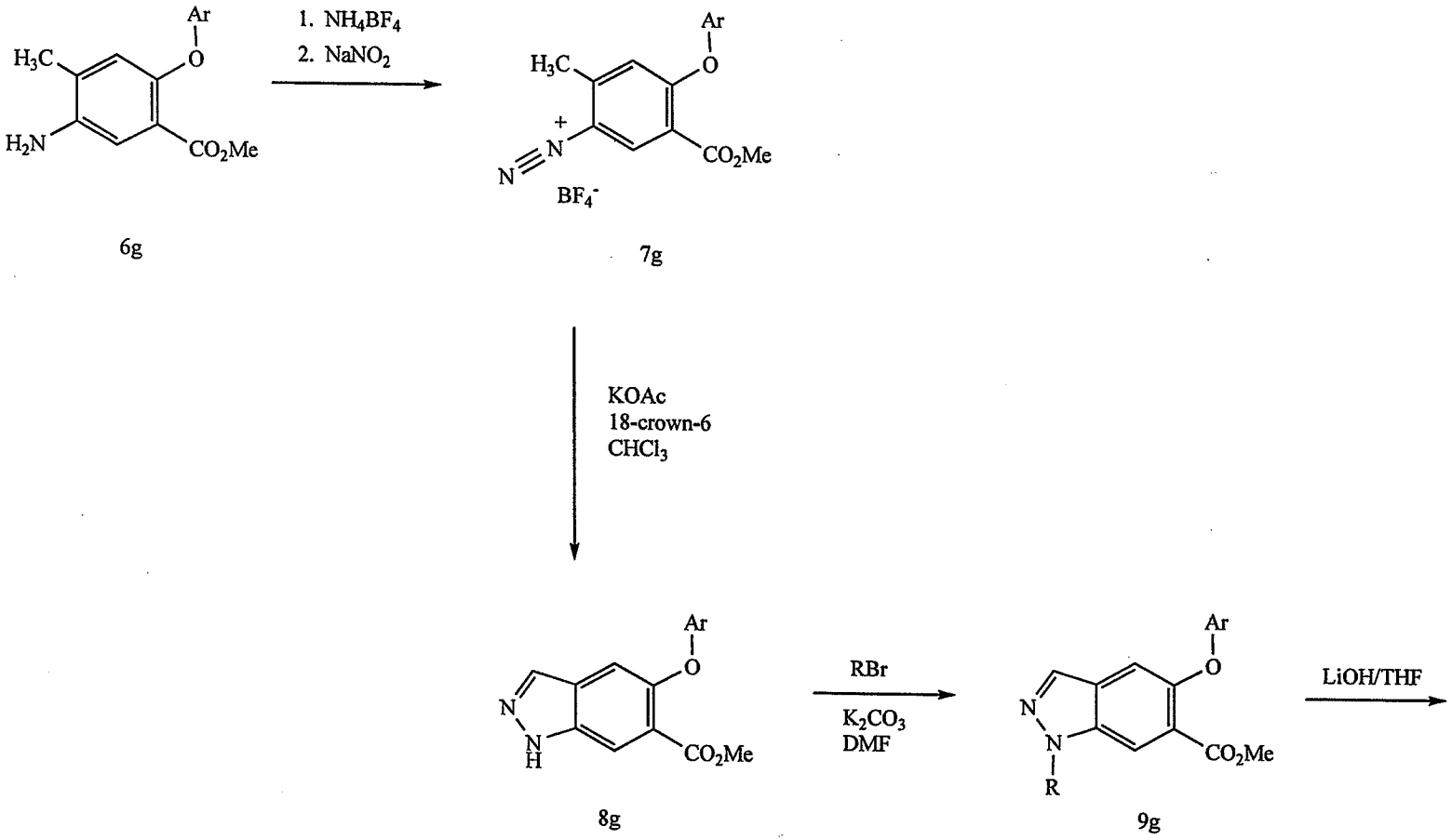
FIG. 54



1g 2g 3g

4g 5g

FIG. 1A

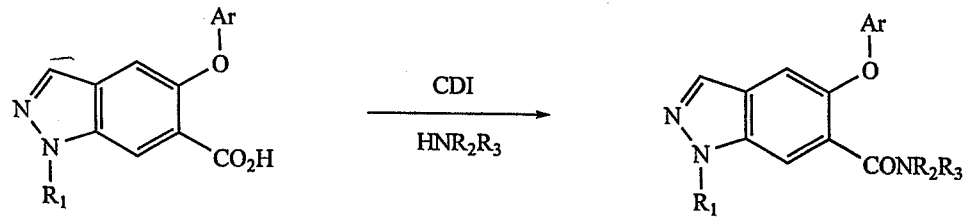


9g-1: $R_1 = CH_2CH(CH_3)_2$

9g-2: $R_2 = CH_2CF_3$

9g-3: $R_1 = CH_3$

FIG. 1B



10g 11g

10g-1: $R_1 = CH_2CH(CH_3)_2$

10g-2: $R_1 = CH_2CF_3$

10g-3: $R_1 = CH_3$

10g-4: $R_1 = H$

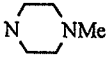
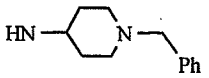
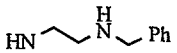
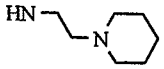
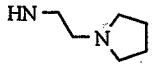
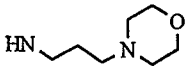
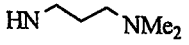
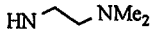
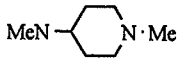
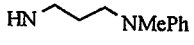
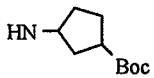
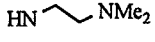
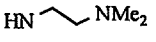
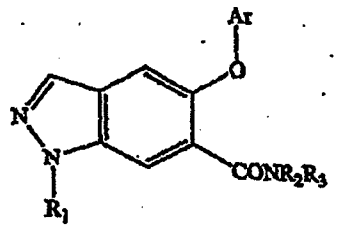
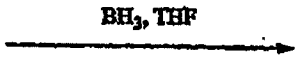
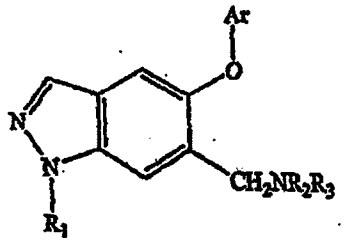
	R_1	NR_2R_3
11g-1:	$CH_2CH(CH_3)_2$	NH_2
11g-2:	$CH_2CH(CH_3)_2$	
11g-3:	$CH_2CH(CH_3)_2$	
11g-4:	$CH_2CH(CH_3)_2$	
11g-5:	$CH_2CH(CH_3)_2$	
11g-6:	$CH_2CH(CH_3)_2$	
11g-7:	$CH_2CH(CH_3)_2$	
11g-8:	$CH_2CH(CH_3)_2$	
11g-9:	$CH_2CH(CH_3)_2$	
11g-10:	$CH_2CH(CH_3)_2$	
11g-11:	$CH_2CH(CH_3)_2$	
11g-12:	$CH_2CH(CH_3)_2$	
11g-13:	$CH_2CH(CH_3)_2$	
11g-14:	CH_2CF_3	
11g-15:	CH_3	
11g-16:	H	

FIG. 1C



11g



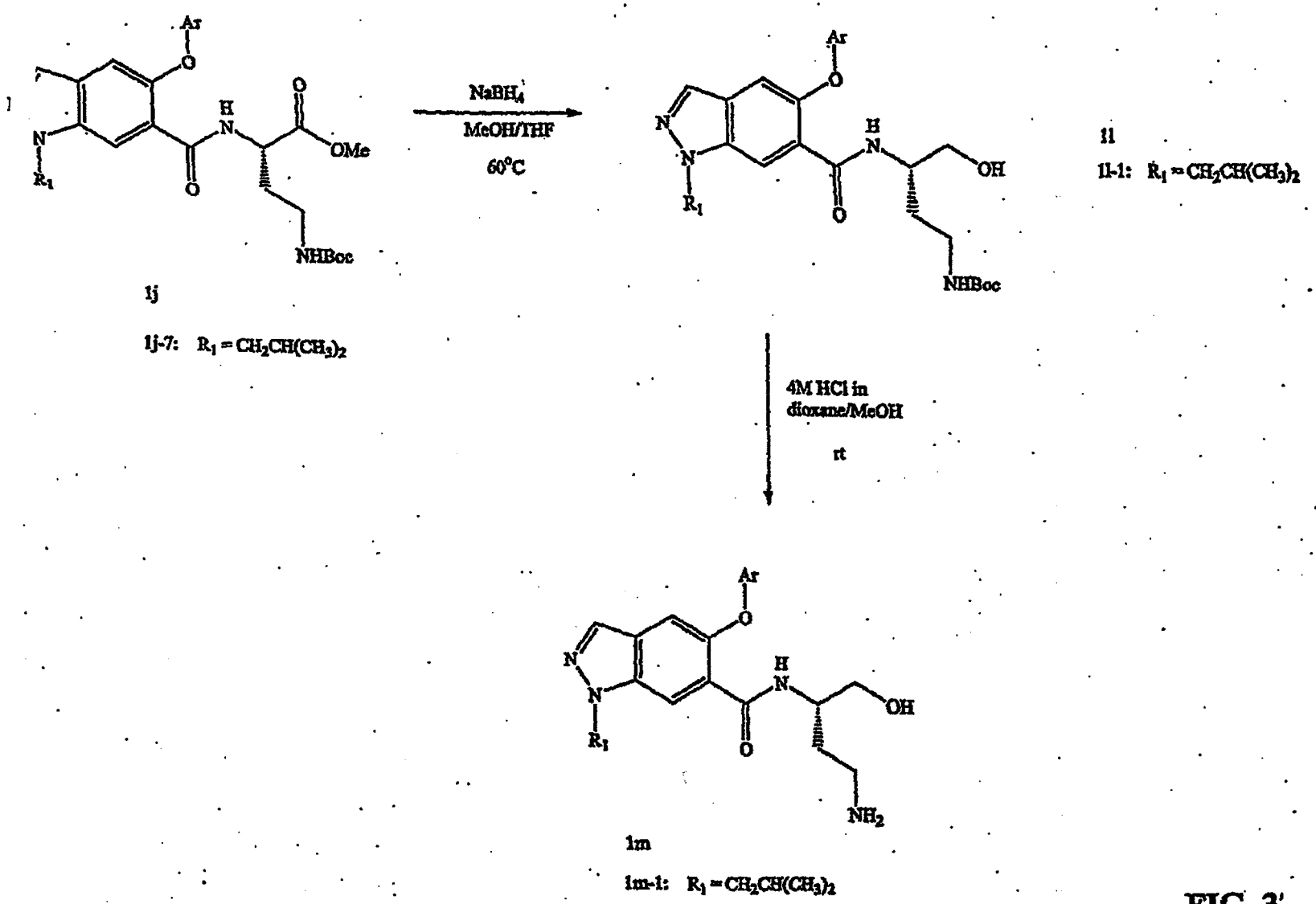


1k

	R_1	R_2	R_3
11g-10:	$CH_2CH(CH_3)_2$	H	

	R_1	R_2	R_3
1k-1:	$CH_2CH(CH_3)_2$	H	
1k-2:	$CH_2CH(CH_3)_2$	SO_2CH_3	
1k-3:	$CH_2CH(CH_3)_2$	$(C=O)CH_3$	

FIG. 2



1j

1j-7: $R_1 = CH_2CH(CH_3)_2$

1l

1l-1: $R_1 = CH_2CH(CH_3)_2$

1m

1m-1: $R_1 = CH_2CH(CH_3)_2$

FIG. 3

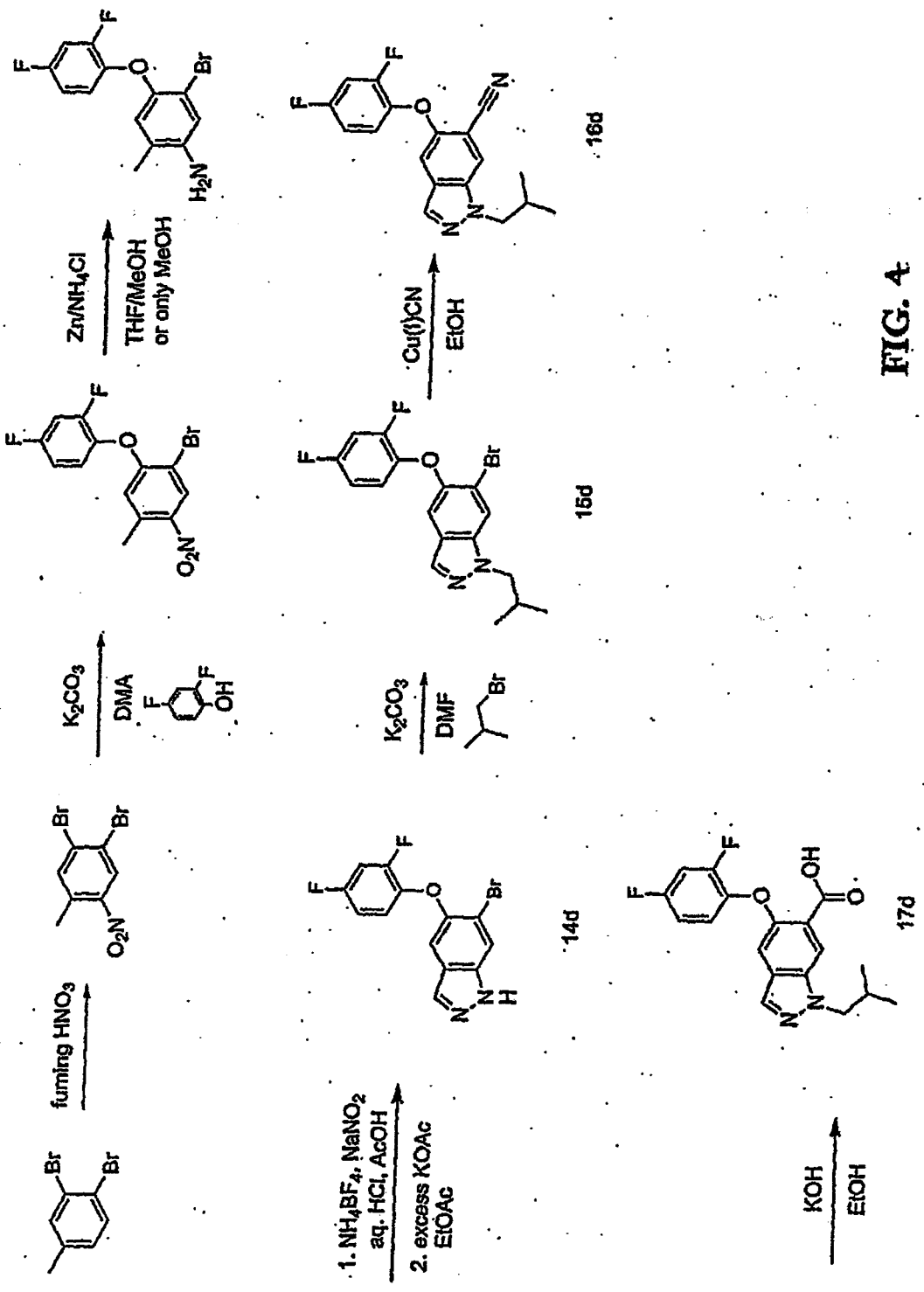

fuming HNO3
K2CO3
DMA
Zn/NH4Cl
THF/MeOH
or only MeOH
1. NH4BF4, NaNO2
aq. HCl, AcOH
2. excess KOAc
EtOAc
K2CO3
DMF
Cu(I)CN
EtOH
KOH
EtOH
14d
15d
16d
17d

FIG. 4

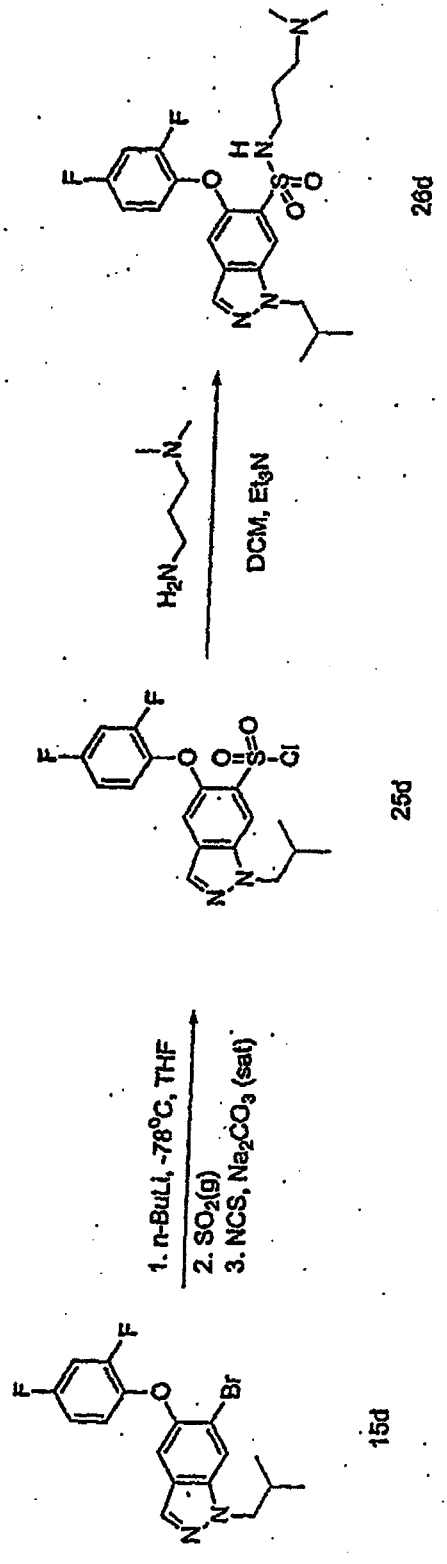


FIG. 5.