Scheme I

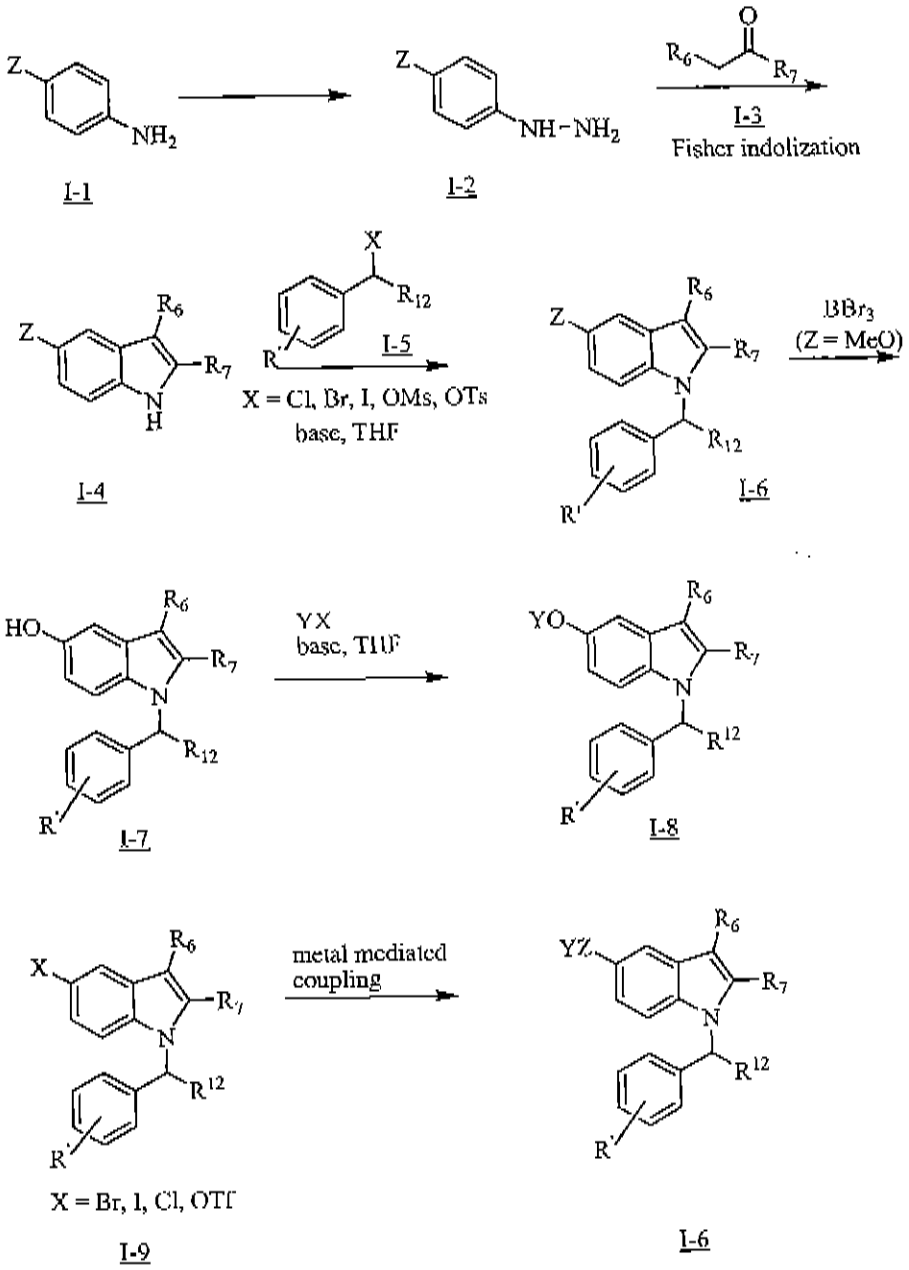
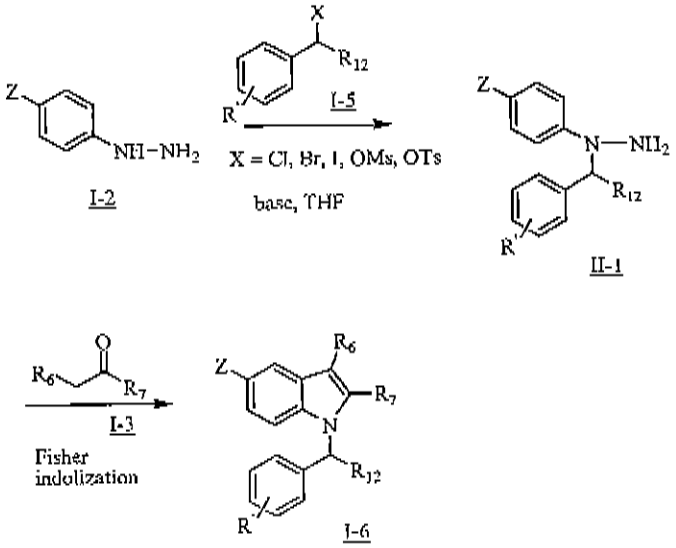


Figure 1

Scheme II



Scheme III

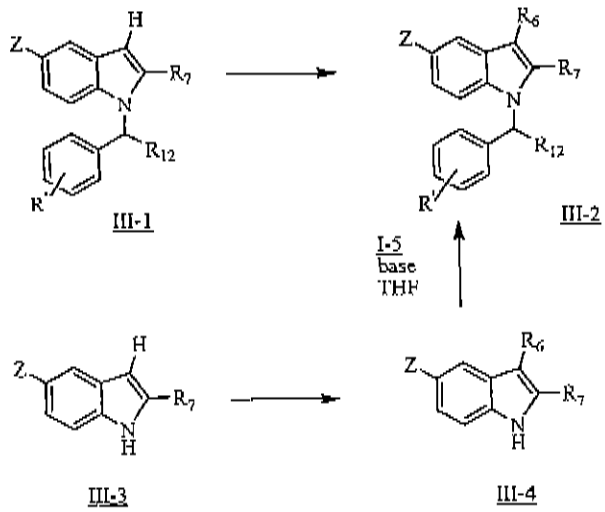
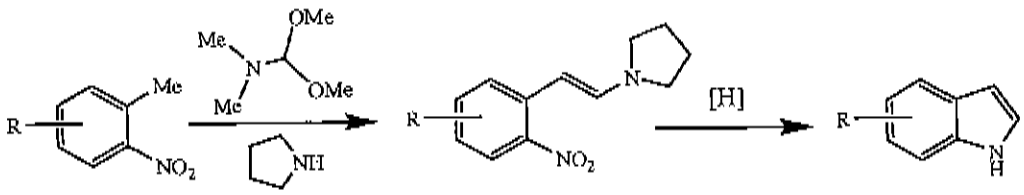
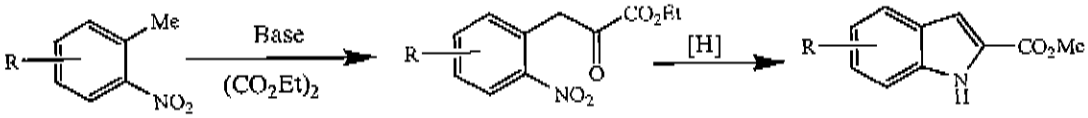


Figure 2

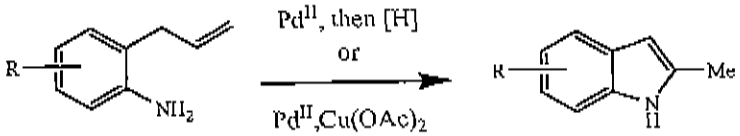
Batcho-Leimgruber Indole Synthesis



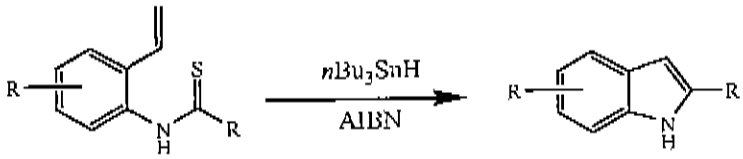
Reissert Indole Synthesis



Hegedus Indole Synthesis



Fukuyama Indole Synthesis



Sugasawa Indole Synthesis

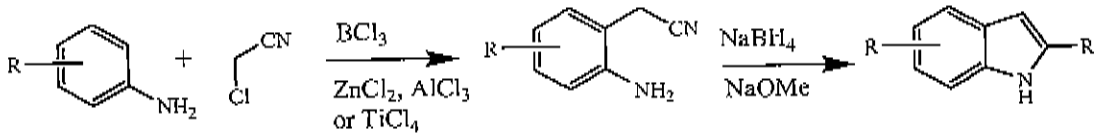
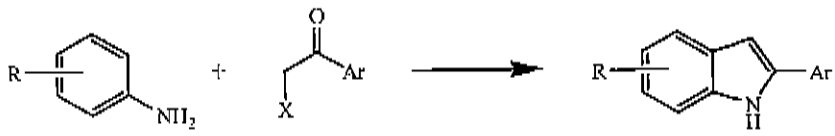
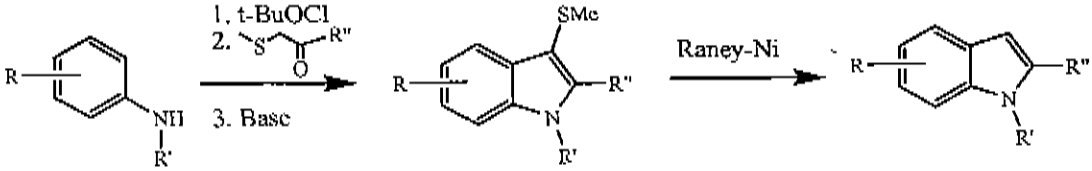


Figure 3

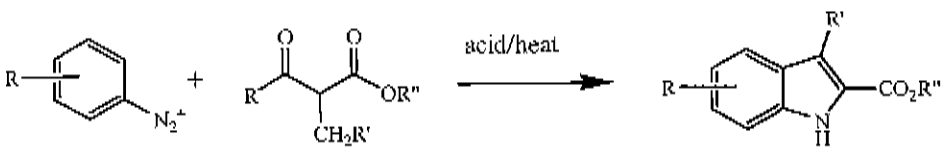
Bischler Indole Synthesis



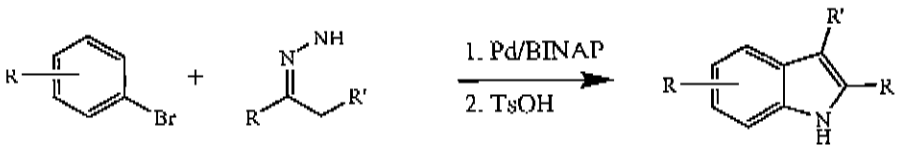
Gassman Indole Synthesis



Japp-Klingemann Indole Synthesis



Buchwald Indole Synthesis



Larock Indole Synthesis

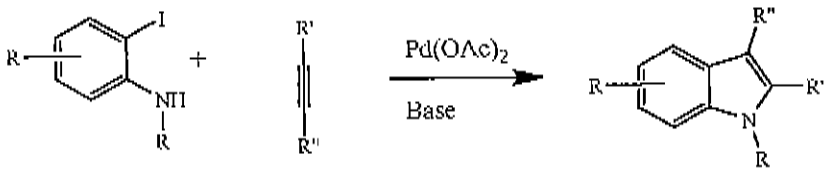
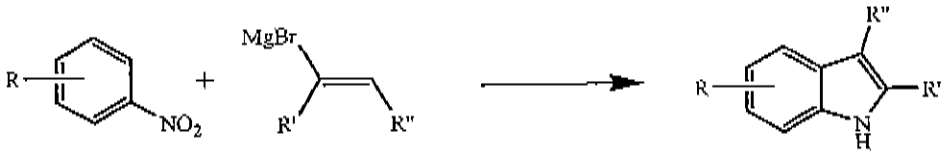
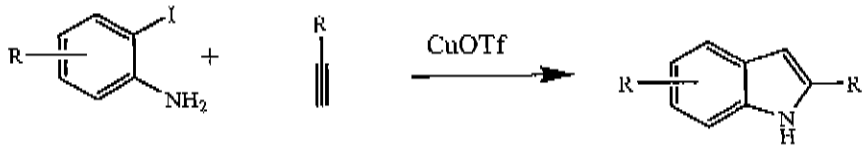


Figure 4

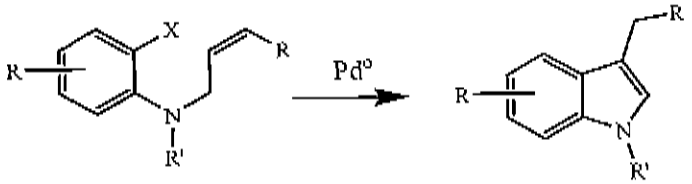
Bartoli Indole Synthesis



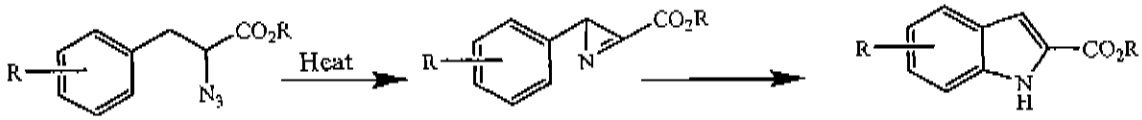
Castro Indole Synthesis



Heck Indole Synthesis



Hemetsberger Indole Synthesis



Mori-Ban Indole Synthesis

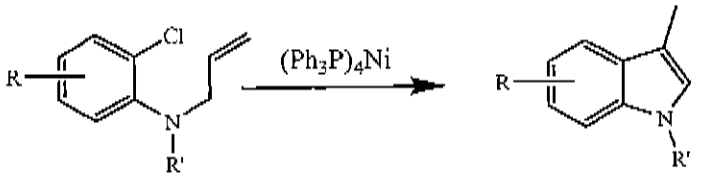
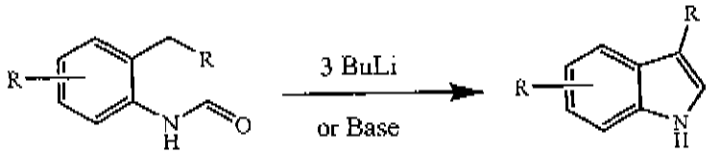
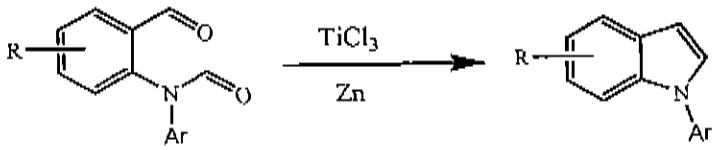


Figure 5

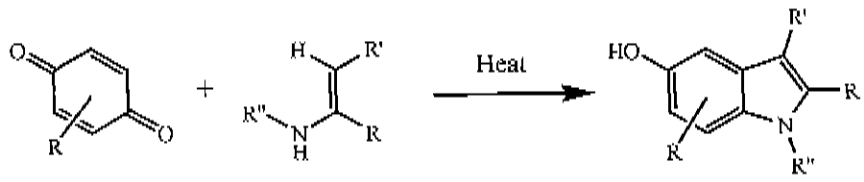
Madelung Indole Synthesis



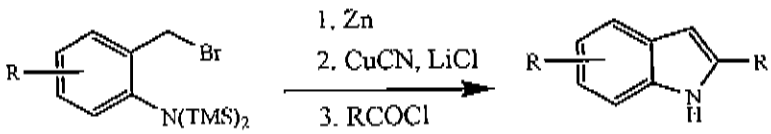
McMurray Indole Synthesis

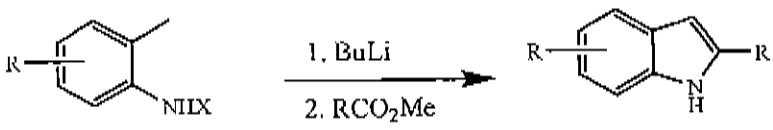


Nenitzescu Indole Synthesis



Other Syntheses

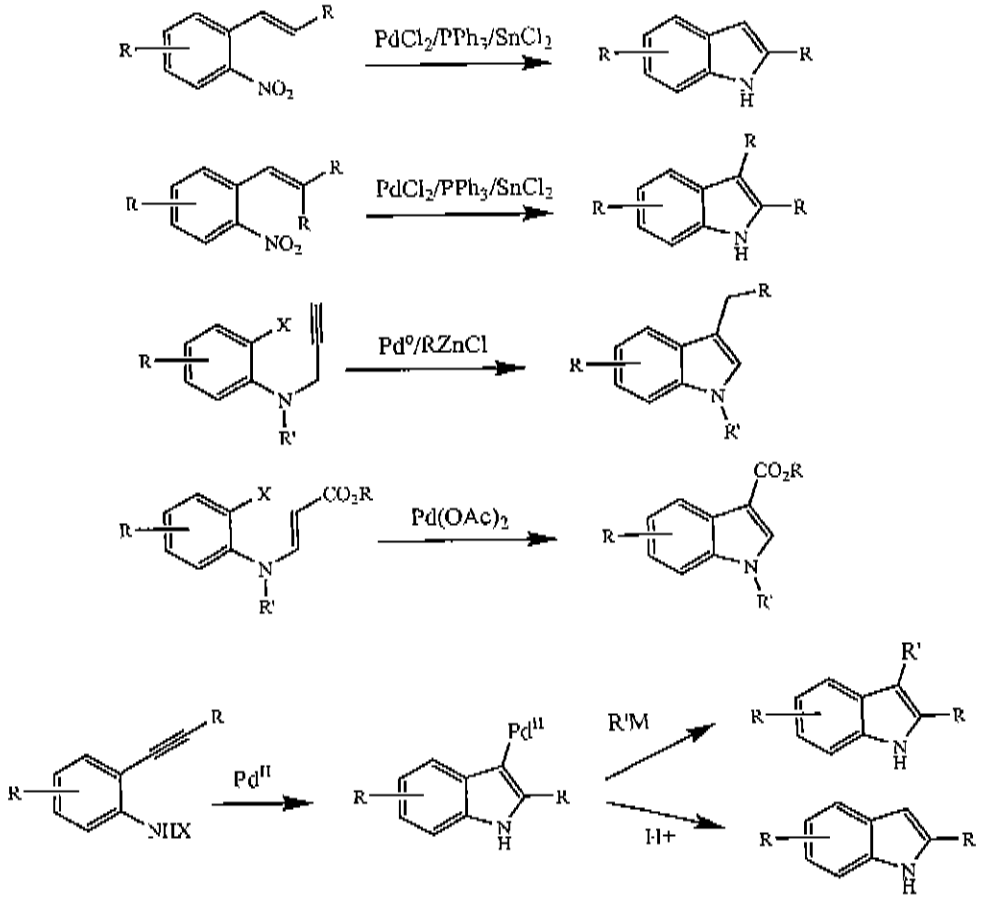




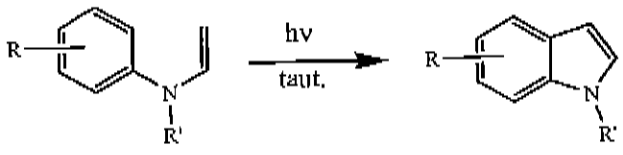
X = TMS, Boc

Figure 6

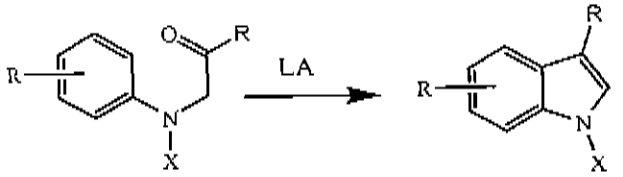
Using Palladium



Photochemical



Acid Catalyzed Cyclization



X = TFA, alkyl. sulfonyl

Figure 7

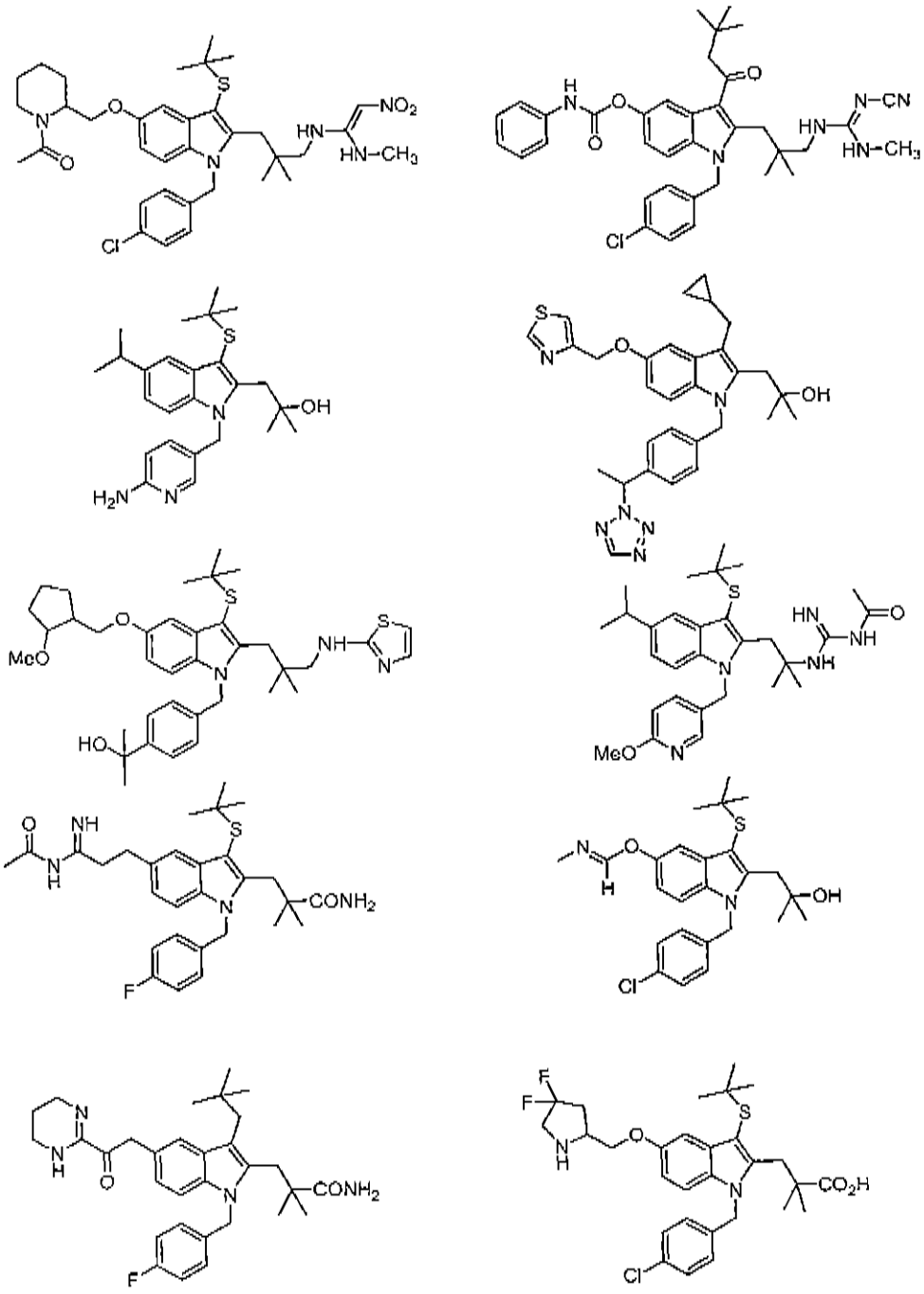


Figure 8

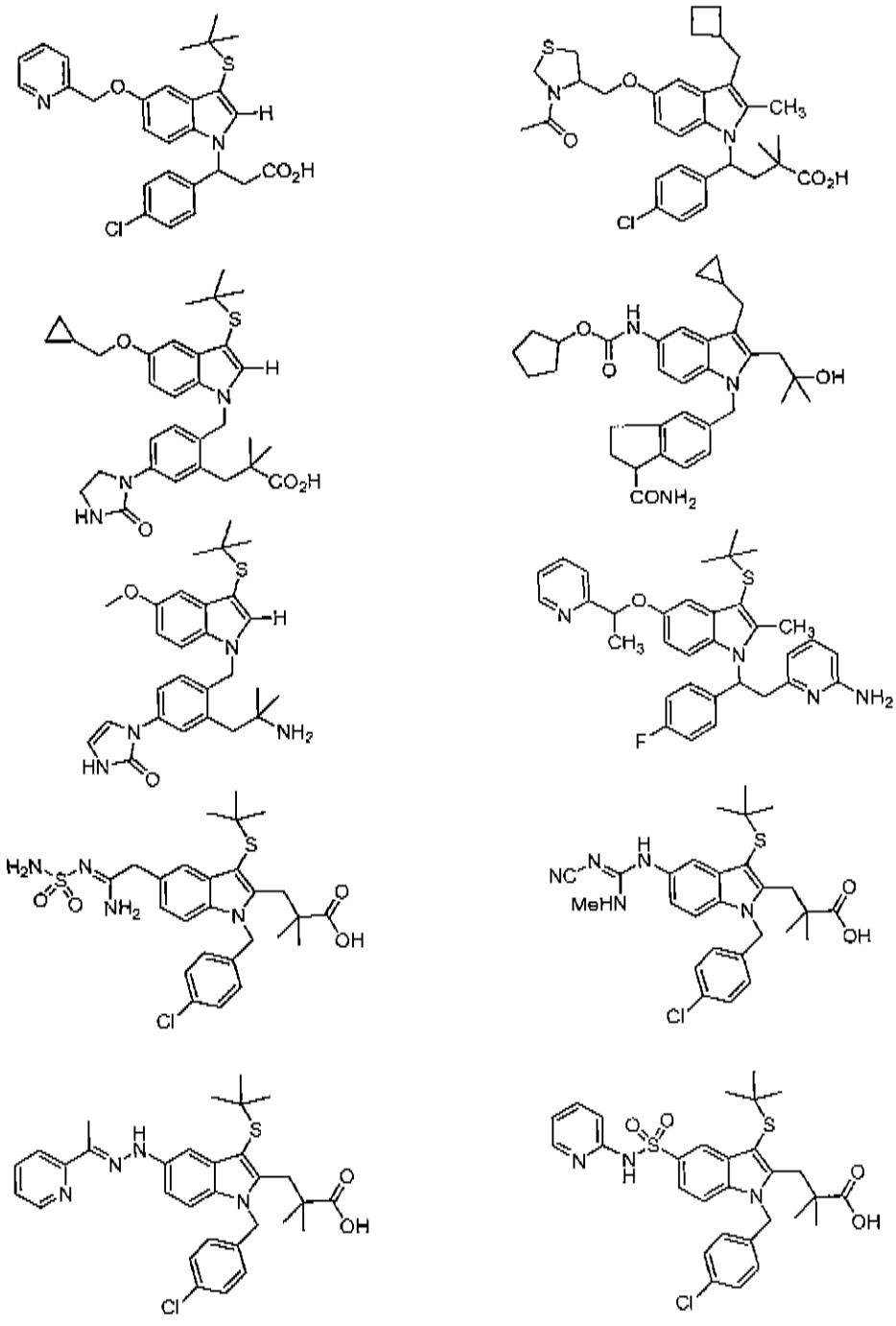


Figure 9

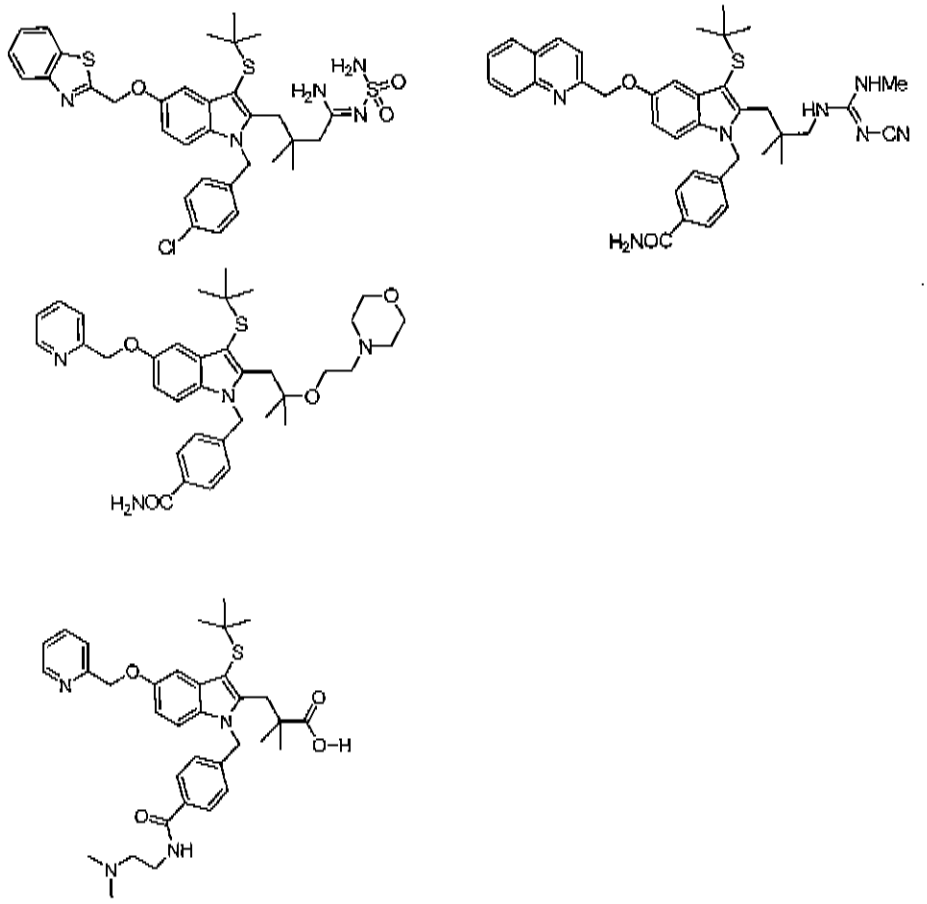


Figure 10

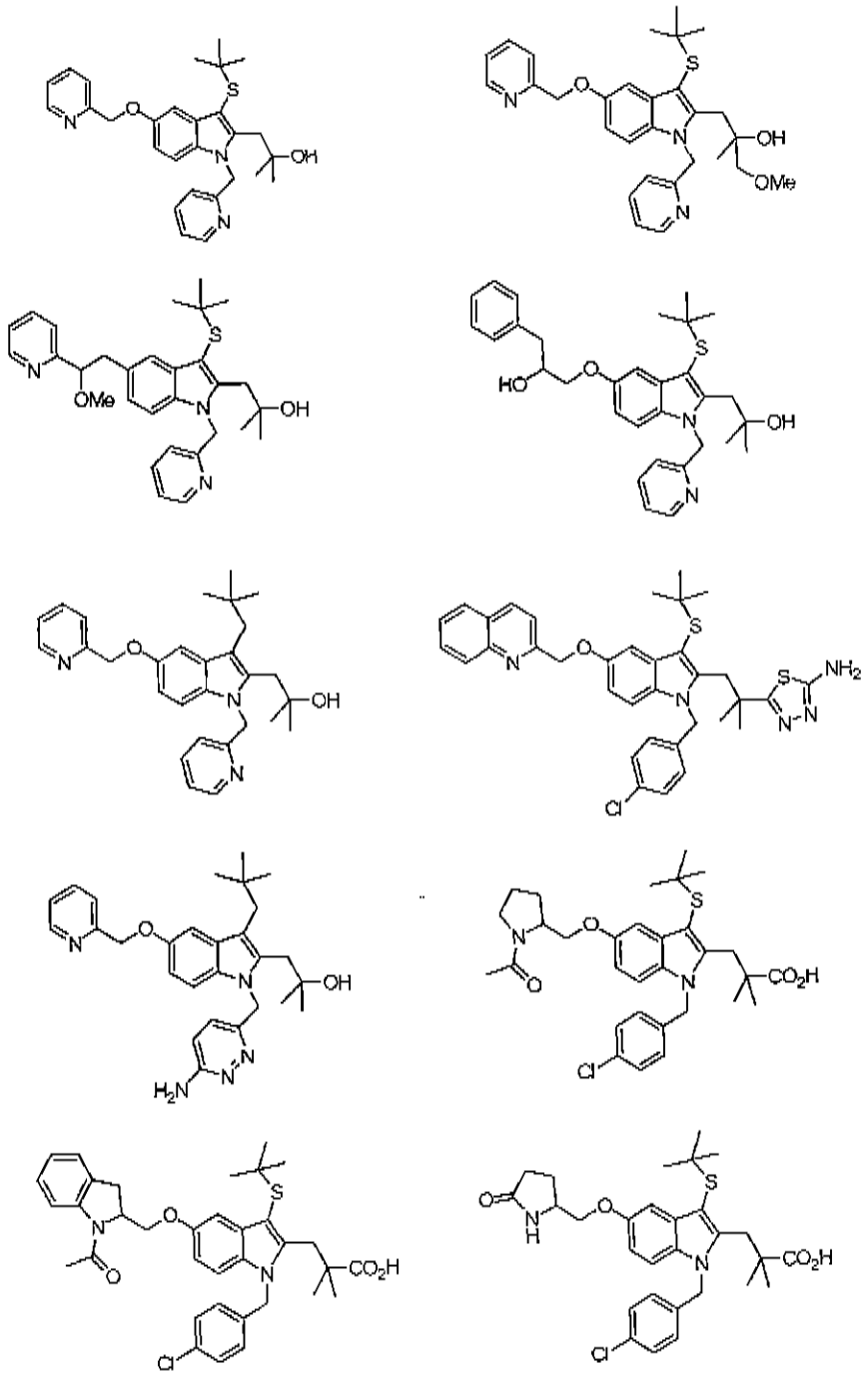


Figure 11

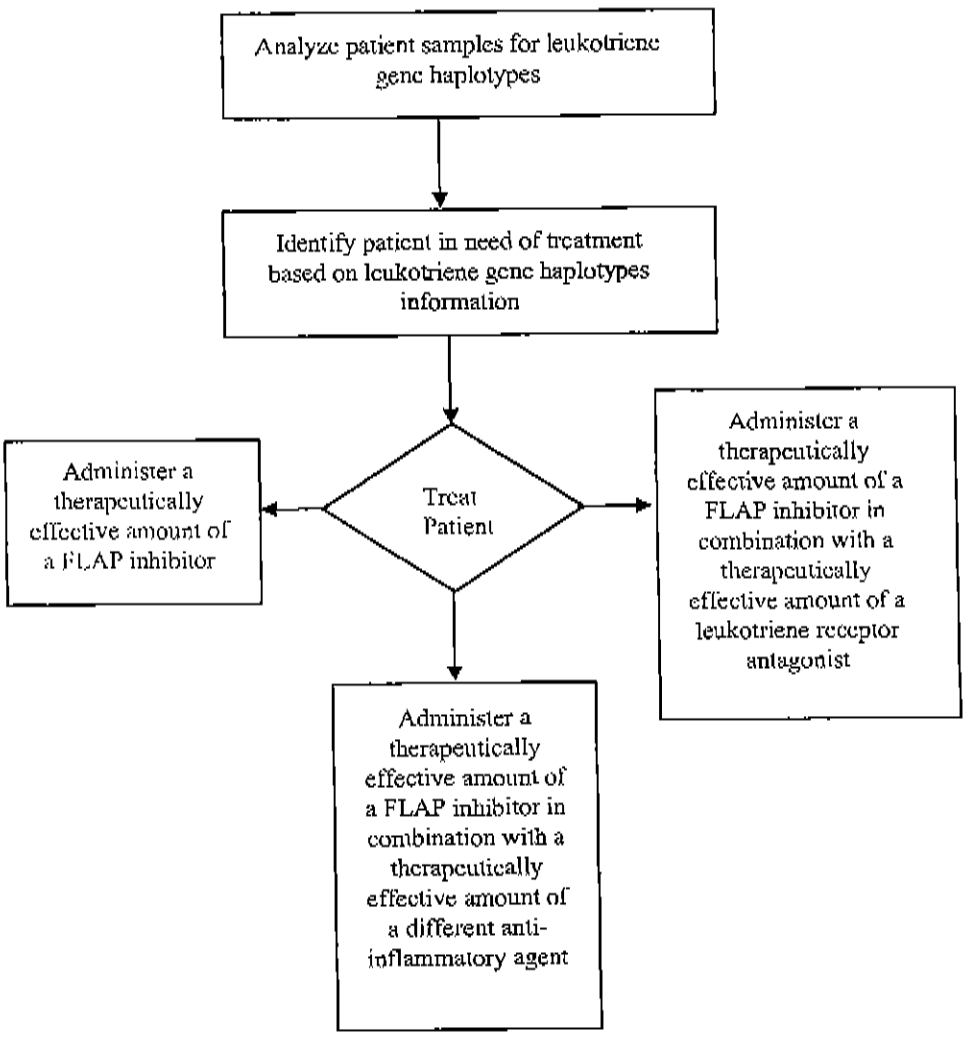

Analyze patient samples for leukotriene gene haplotypes
Identify patient in need of treatment based on leukotriene gene haplotypes information
Treat Patient
Administer a therapeutically effective amount of a FLAP inhibitor
Administer a therapeutically effective amount of a FLAP inhibitor in combination with a therapeutically effective amount of a leukotriene receptor antagonist
Administer a therapeutically effective amount of a FLAP inhibitor in combination with a therapeutically effective amount of a different anti-inflammatory agent

Figure 12

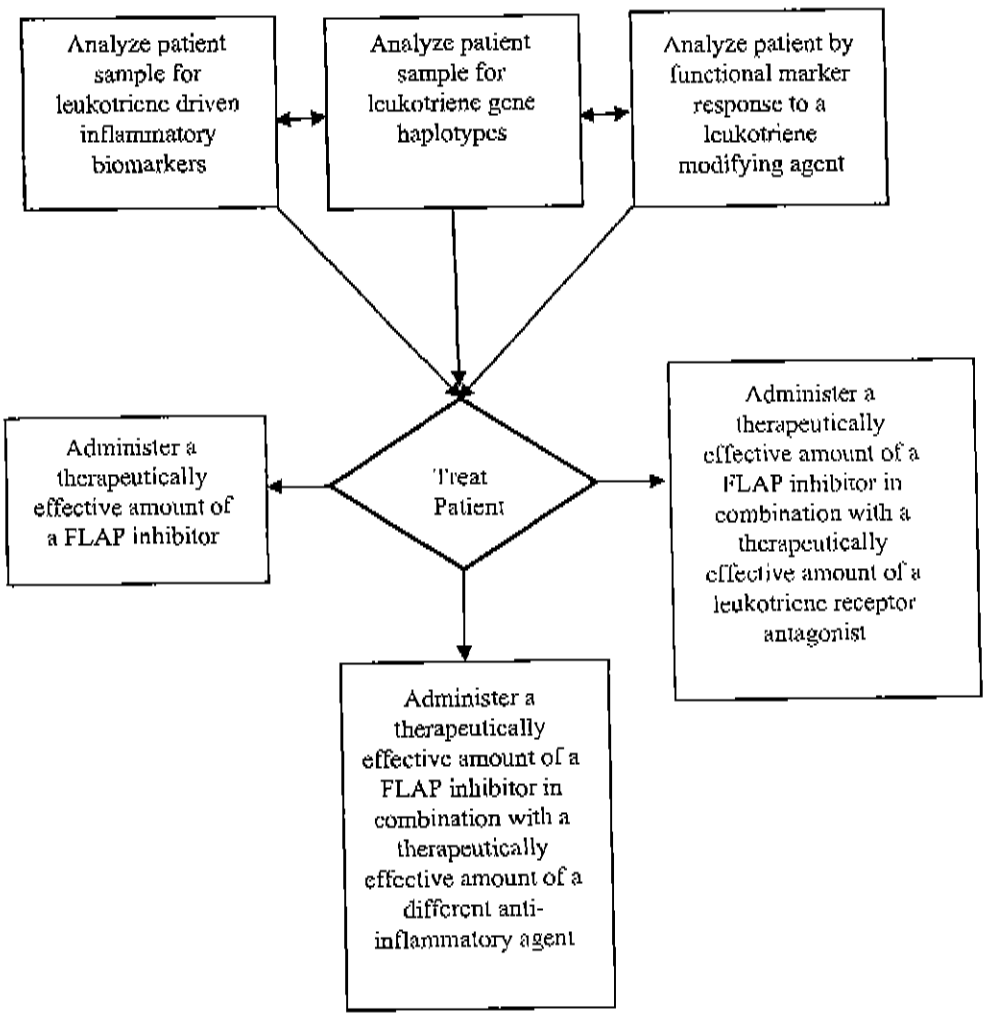

Analyze patient sample for leukotriene driven inflammatory biomarkers
Analyze patient sample for leukotriene gene haplotypes
Analyze patient by functional marker response to a leukotriene modifying agent
Treat Patient
Administer a therapeutically effective amount of a FLAP inhibitor
Administer a therapeutically effective amount of a FLAP inhibitor in combination with a therapeutically effective amount of a leukotriene receptor antagonist
Administer a therapeutically effective amount of a FLAP inhibitor in combination with a therapeutically effective amount of a different anti-inflammatory agent

Figure 13

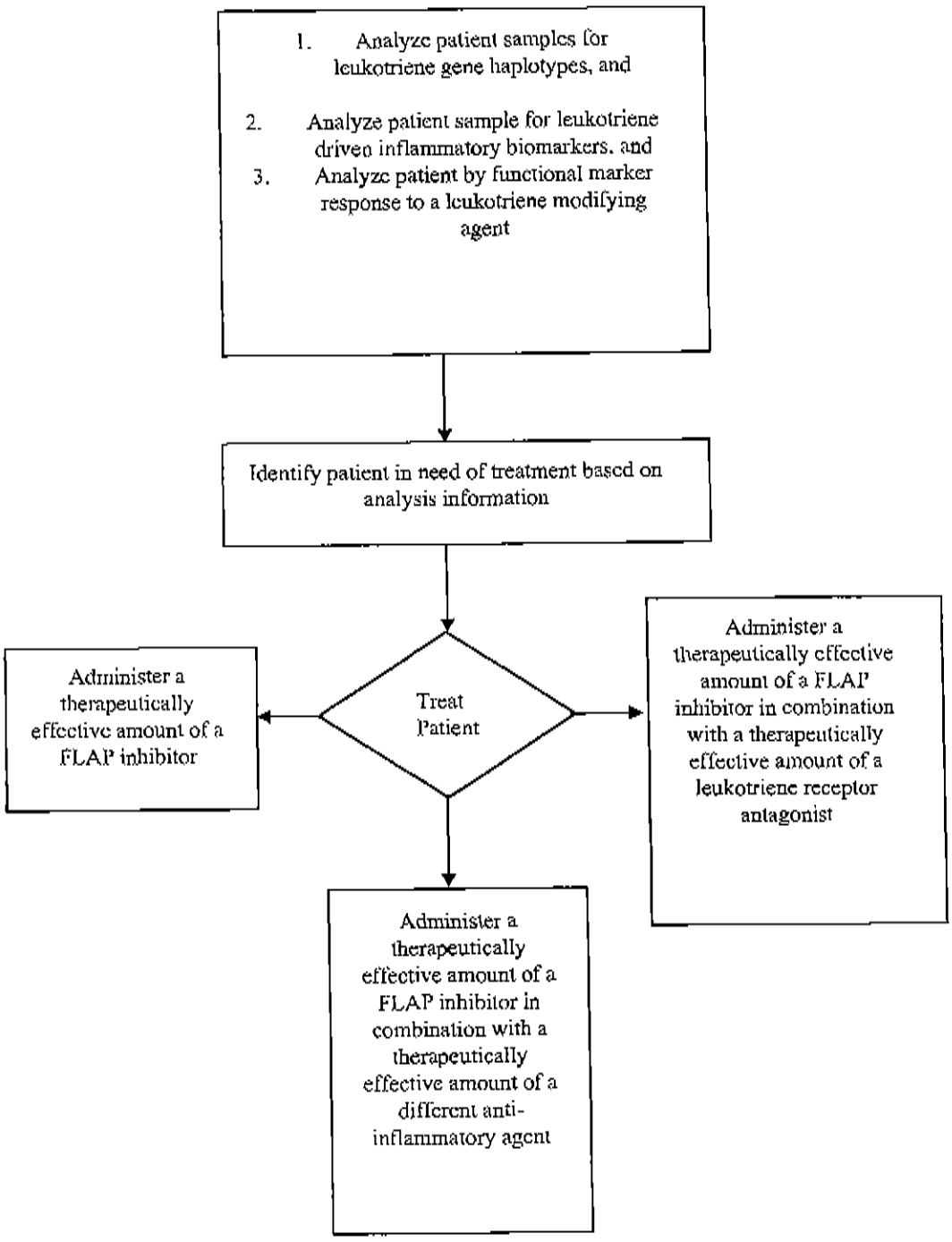

1. Analyze patient samples for leukotriene gene haplotypes, and
2. Analyze patient sample for leukotriene driven inflammatory biomarkers, and
3. Analyze patient by functional marker response to a leukotriene modifying agent
Identify patient in need of treatment based on analysis information
Treat Patient
Administer a therapeutically effective amount of a FLAP inhibitor
Administer a therapeutically effective amount of a FLAP inhibitor in combination with a therapeutically effective amount of a leukotriene receptor antagonist
Administer a therapeutically effective amount of a FLAP inhibitor in combination with a therapeutically effective amount of a different anti-inflammatory agent

Figure 14

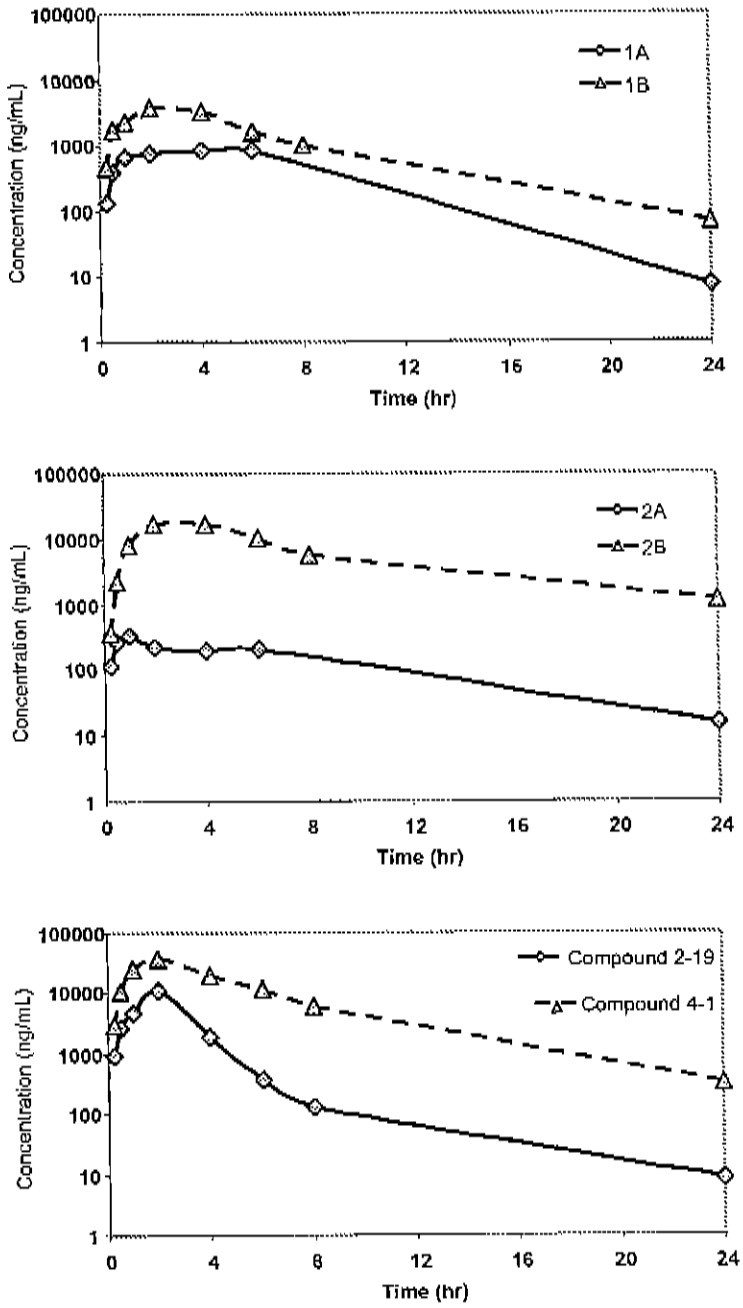

100000
10000
1000
100
10
1
Concentration (ng/mL)
0
4
8
12
16
20
24
Time (hr)
1A
1B
2A
2B
Compound 2-19
Compound 4-1

Figure 15