Effect Of Compound 493 in FCA-Induced Hyperalgesia Model of Inflammatory Pain at 1 h Post Dosing

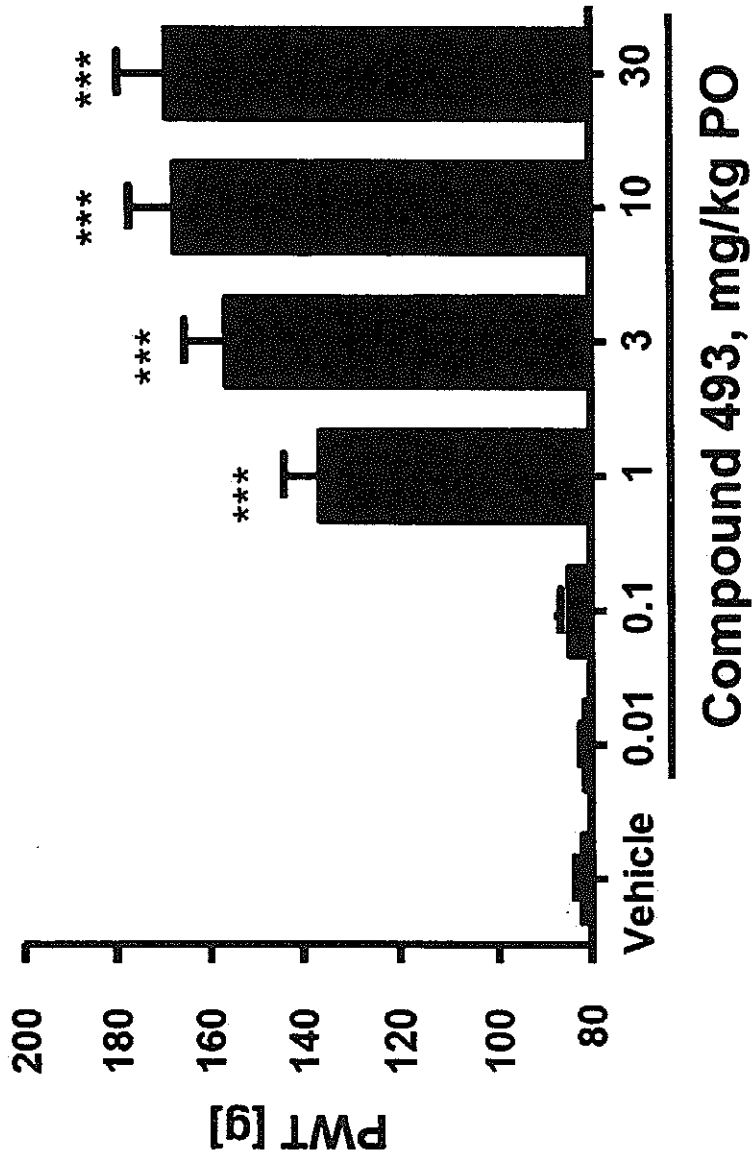


Figure 1

Effect Of Compound 493 in MIA-Induced Osteoarthritis Pain at 1 h Post Dosing

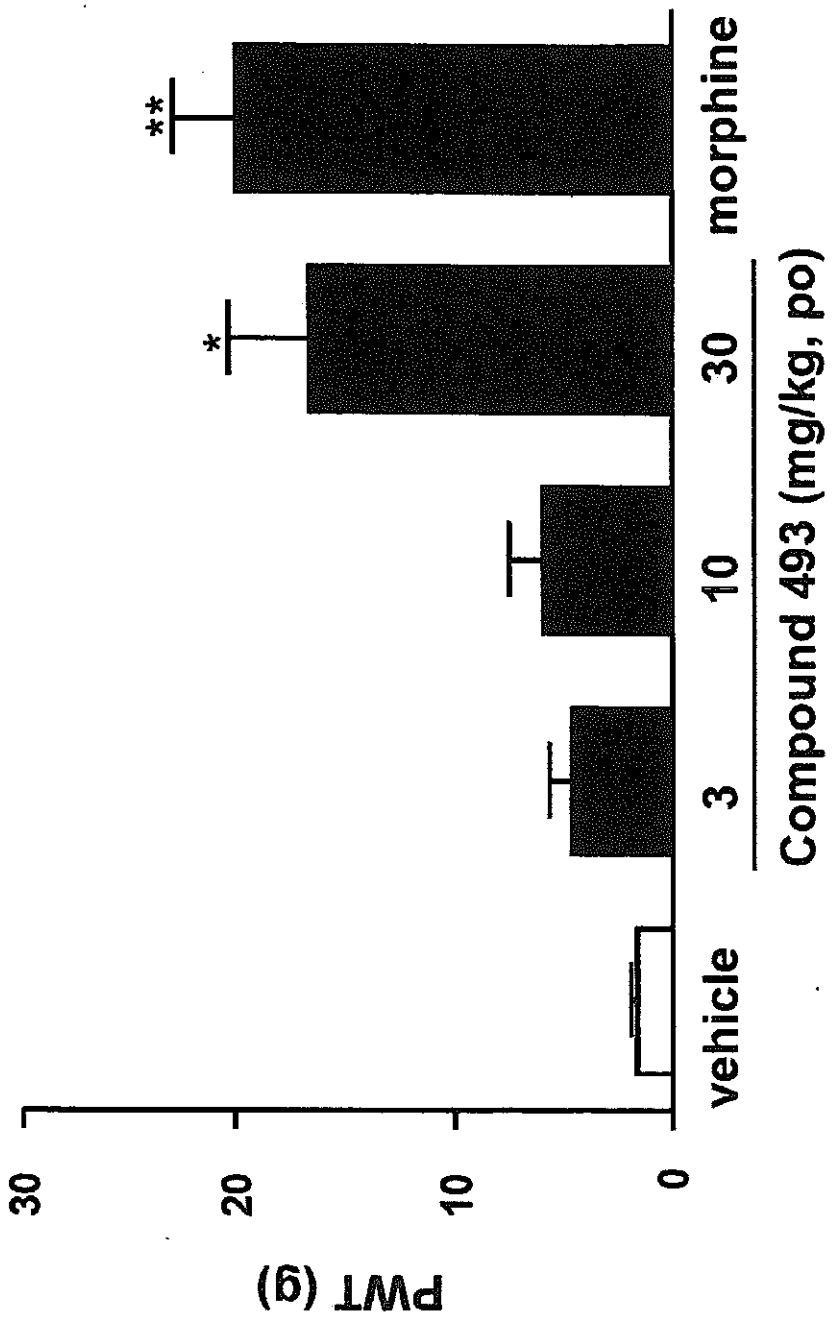


Figure 2

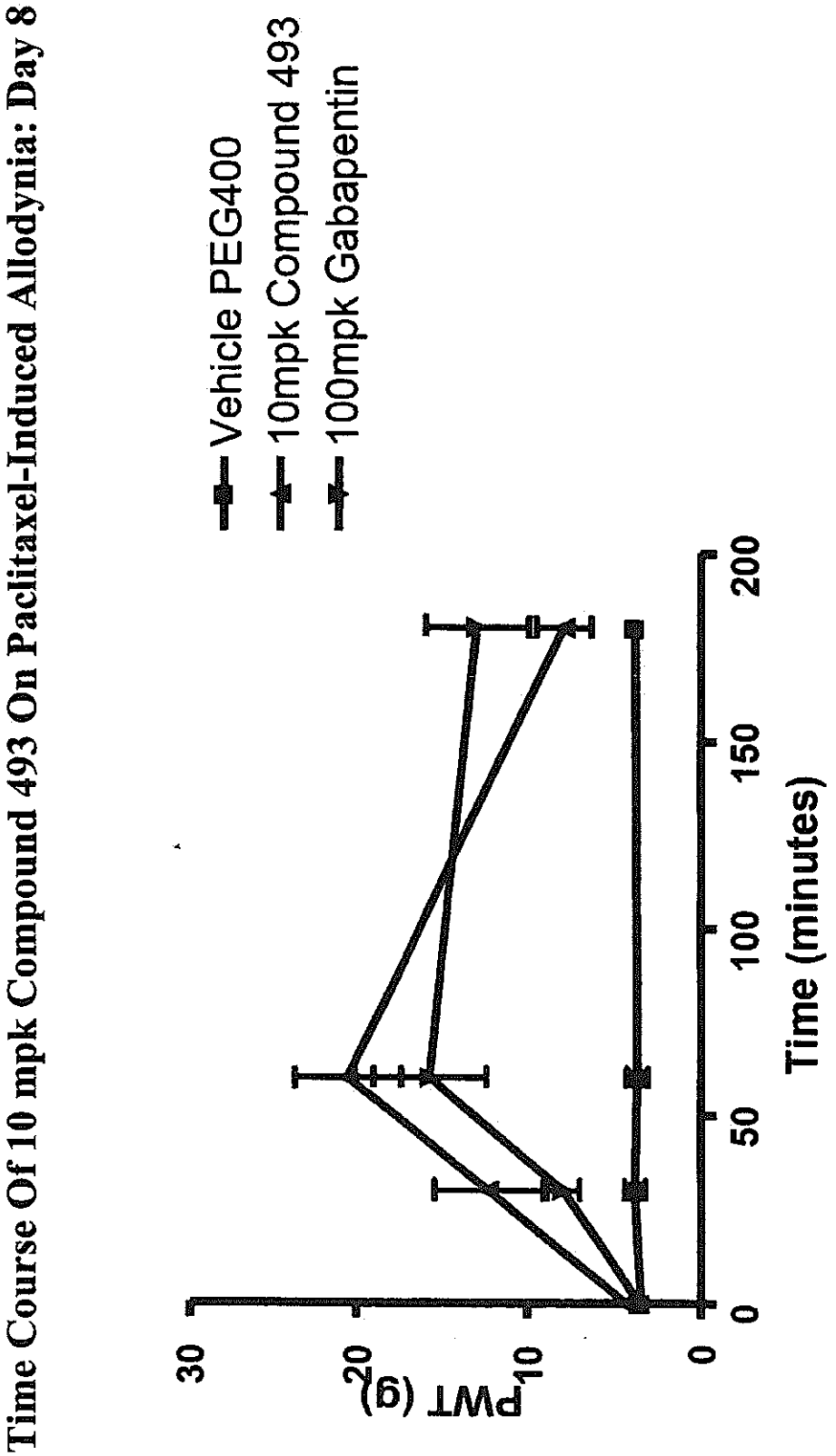
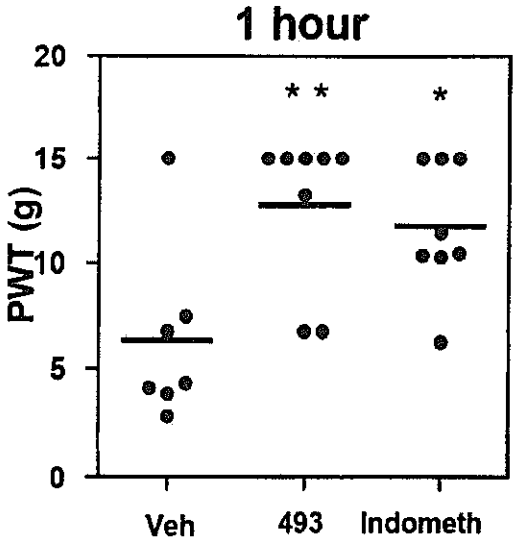

Time Course Of 10 mpk Compound 493 On Paclitaxel-Induced Allodynia: Day 8
Vehicle PEG400
10mpk Compound 493
100mpk Gabapentin
PWT (g)
30
20
10
0
0
50
100
150
200
Time (minutes)

Figure 3

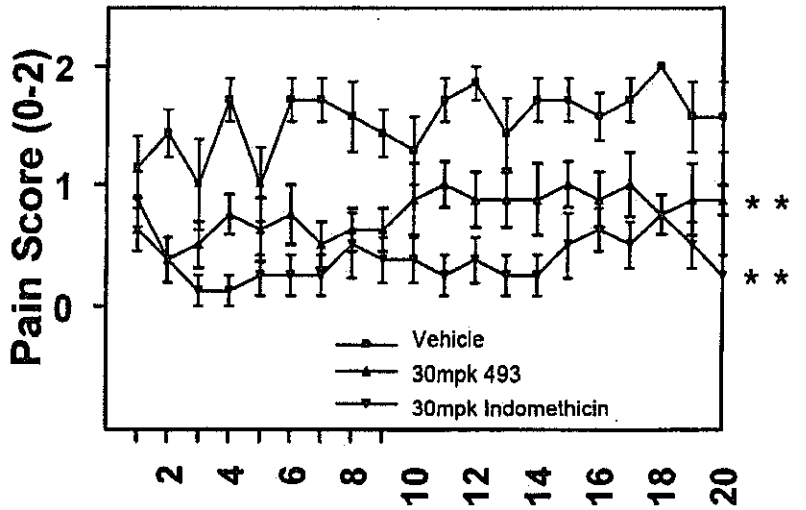
Effect of Compound 493 in Skin Incision Model

Evoked Pain Response



* * P<0.01; * P<0.05 ANOVA followed by Dunnett's multiple comparsion test

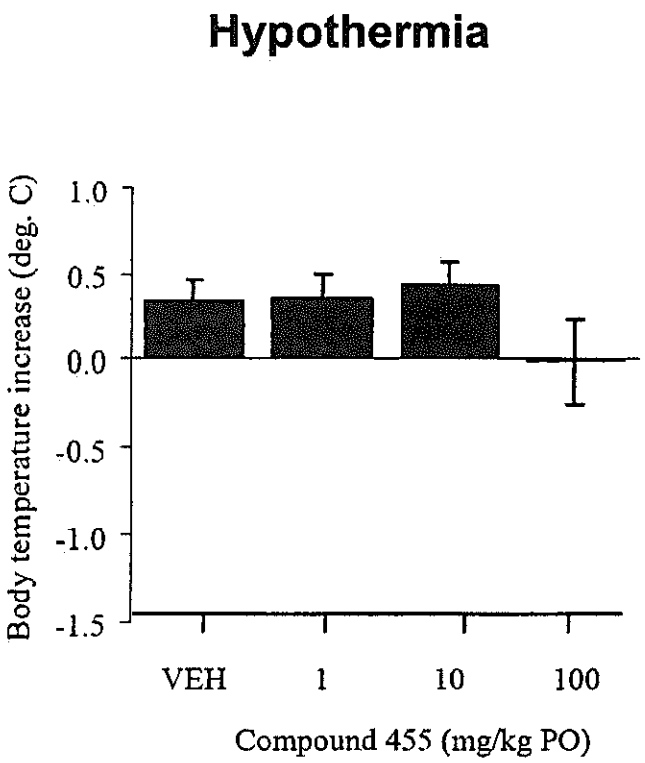
Behavioral Observation



* *P<0.01 ANOVA followed by Dunnett's multiple comparsion test

Figure 4

Effects of Compound 455 on Body Temperature and Locomotor Activity in Rats



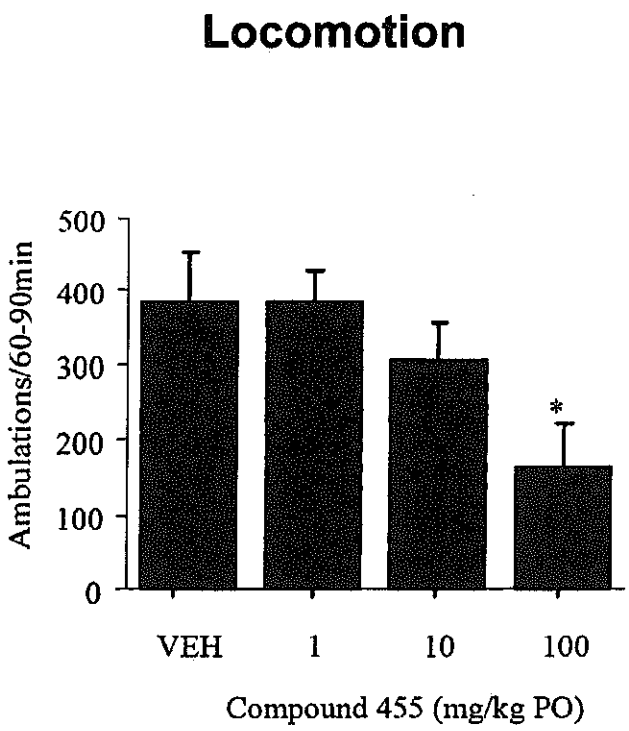


Figure 5

Effects of Compound 660 on Body Temperature and Locomotor Activity in Rats

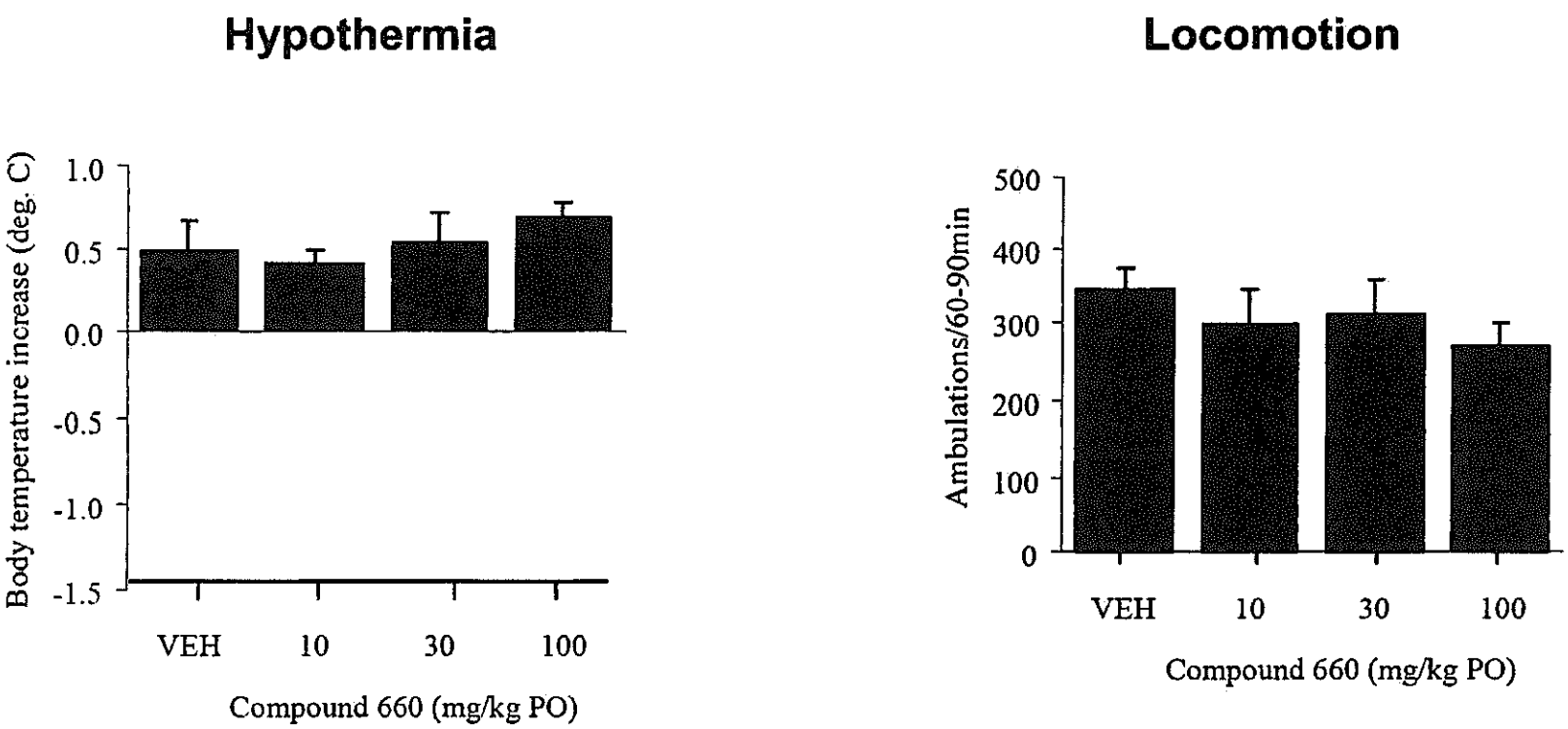


Figure 6

Effects of Compound 700 on Body Temperature and Locomotor Activity in Rats

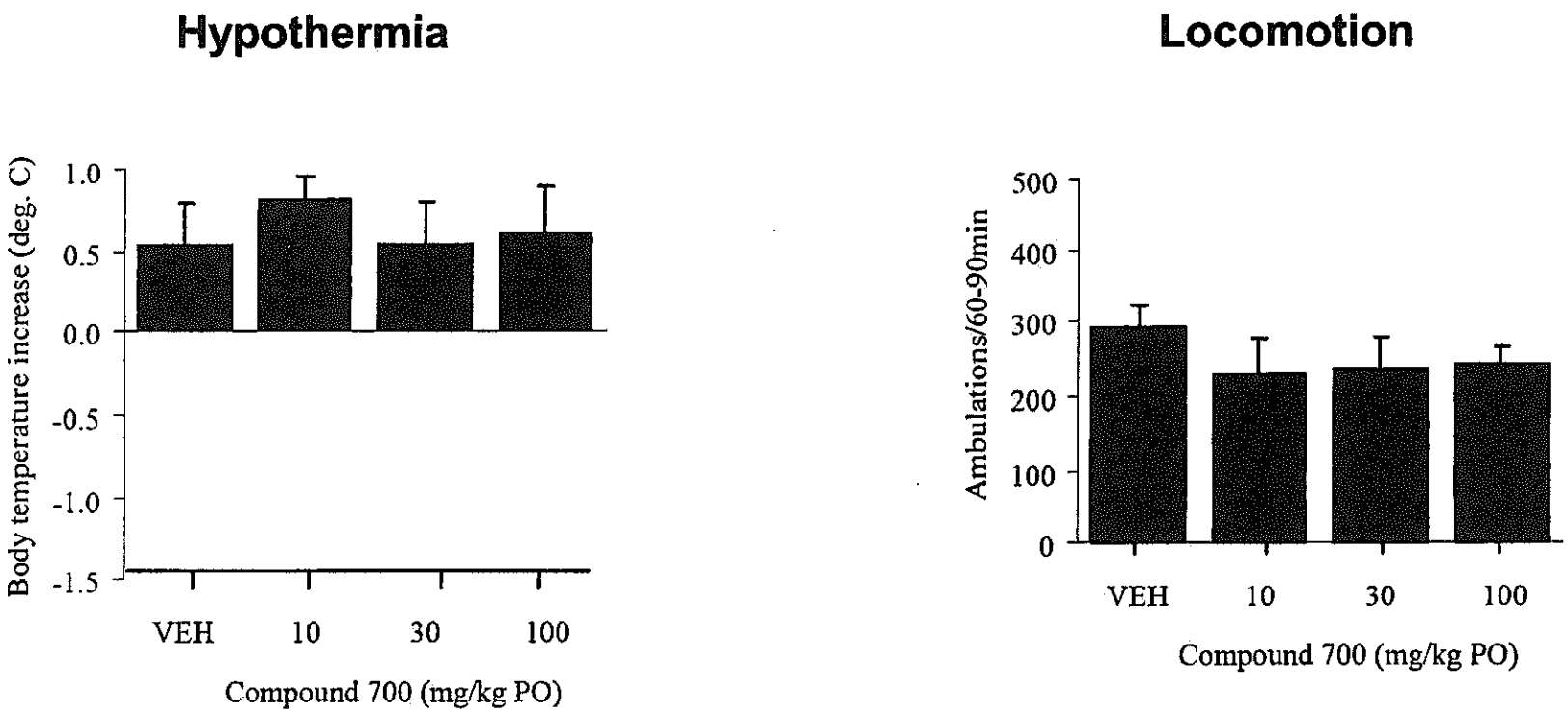


Figure 7

Effects of Compound 667 on Body Temperature and Locomotor Activity in Rats

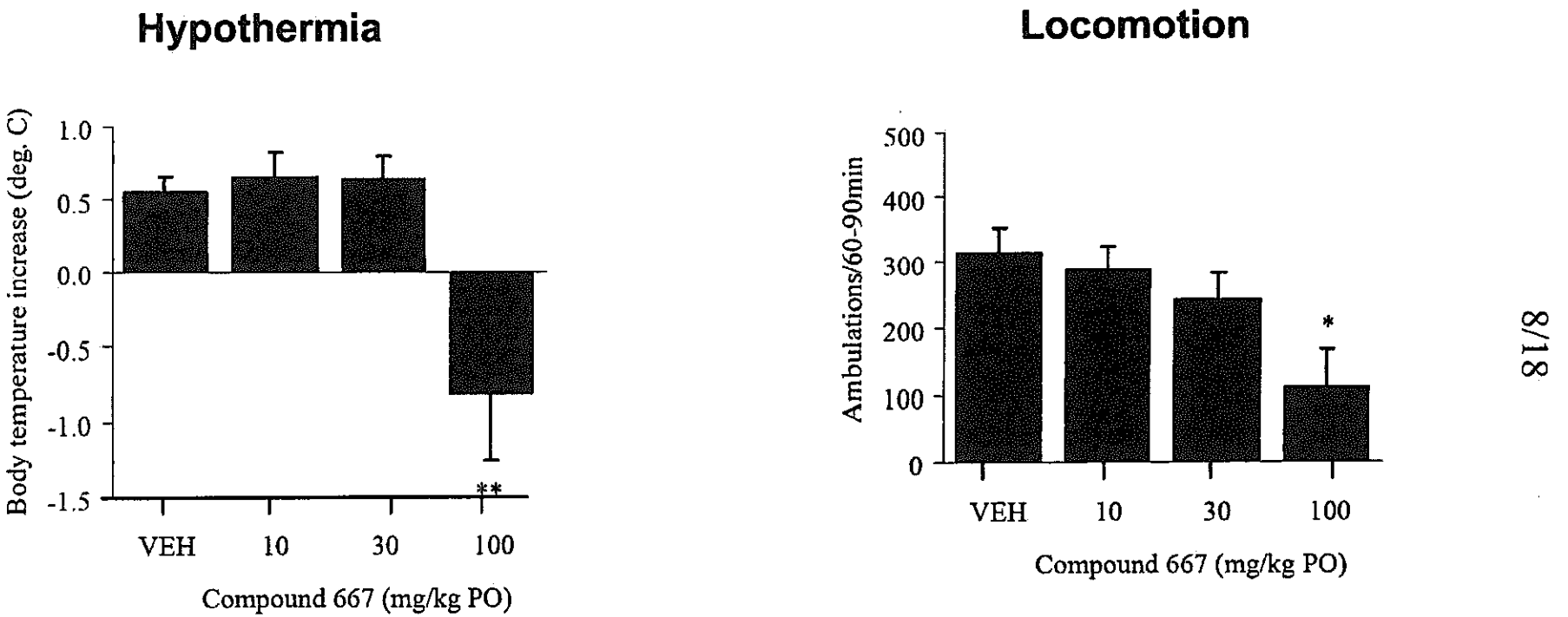


Figure 8

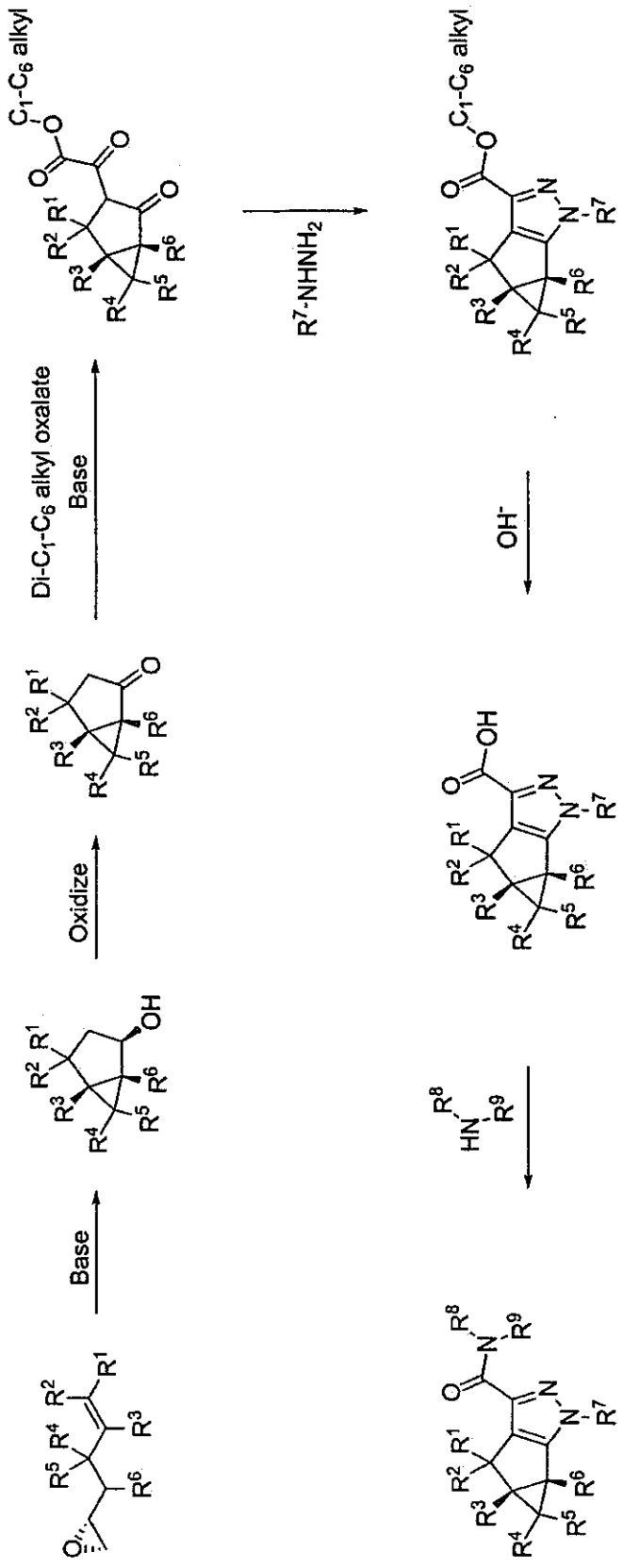

Base
Oxidize
Di-C1-C6 alkyl oxalate
Base
R7-NHNH2
OH-
C1-C6 alkyl

Figure 9

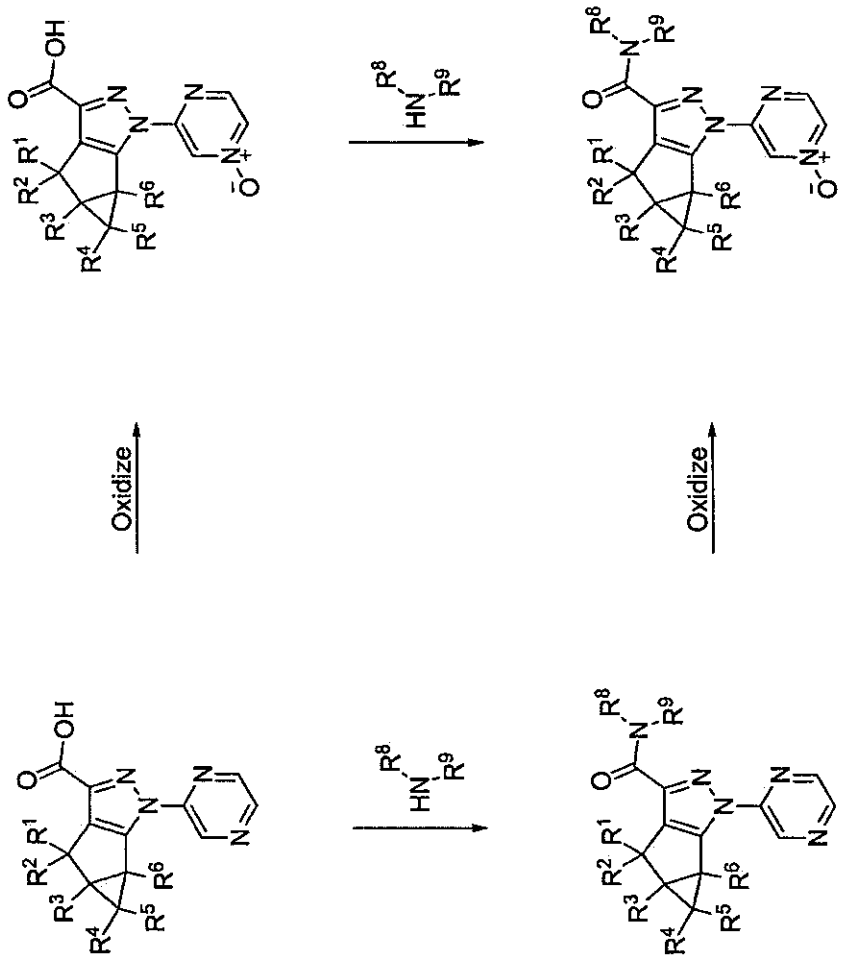


Figure 10

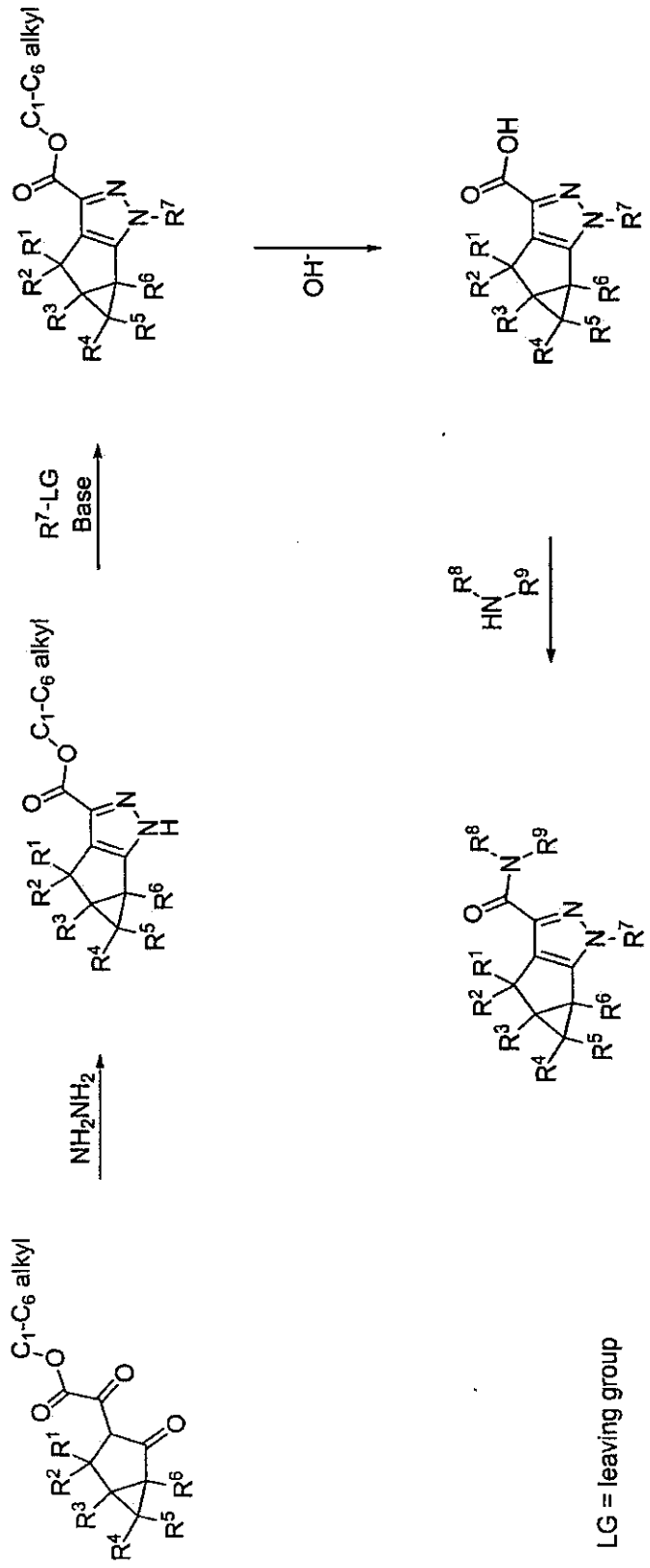


Figure 11

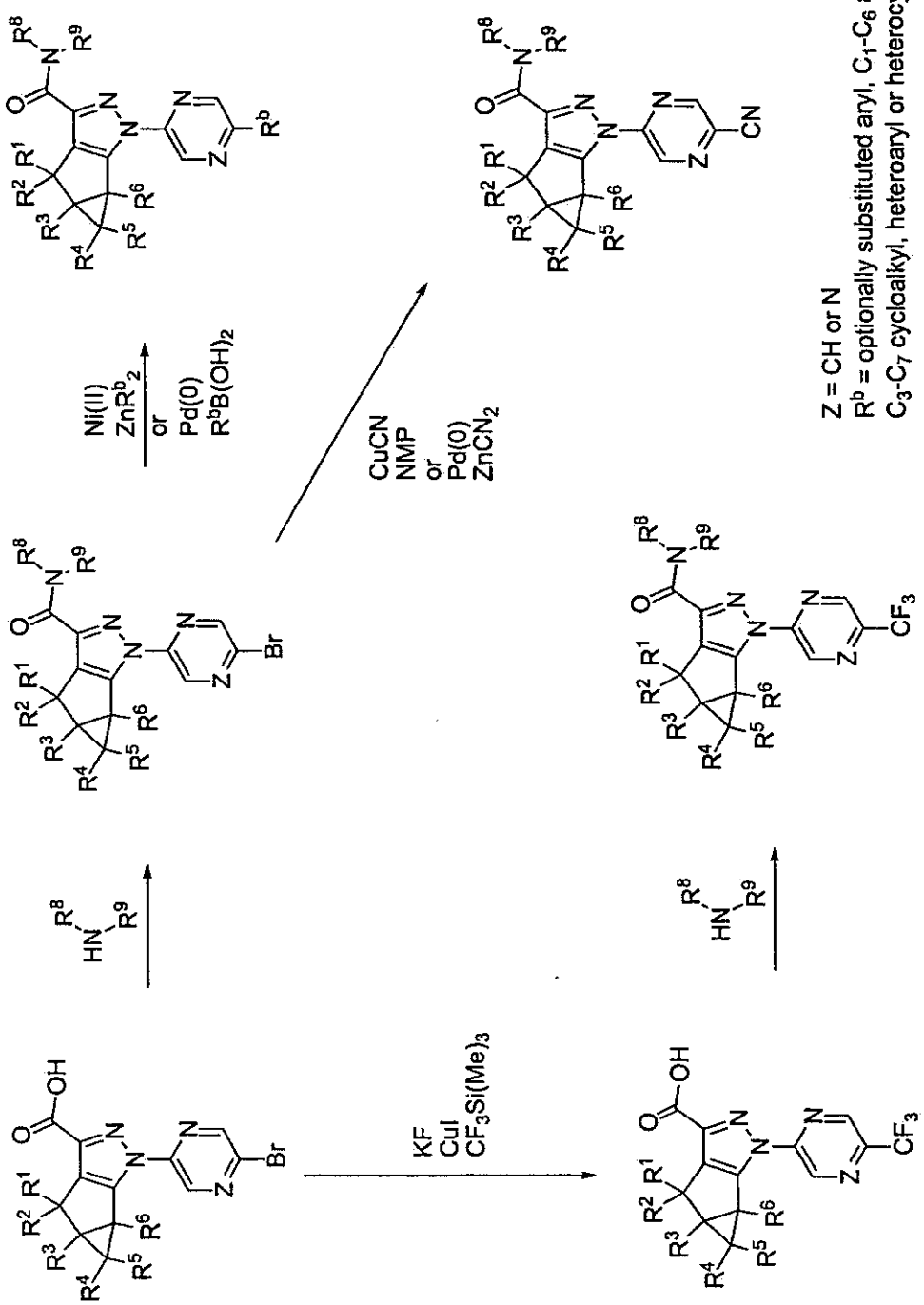
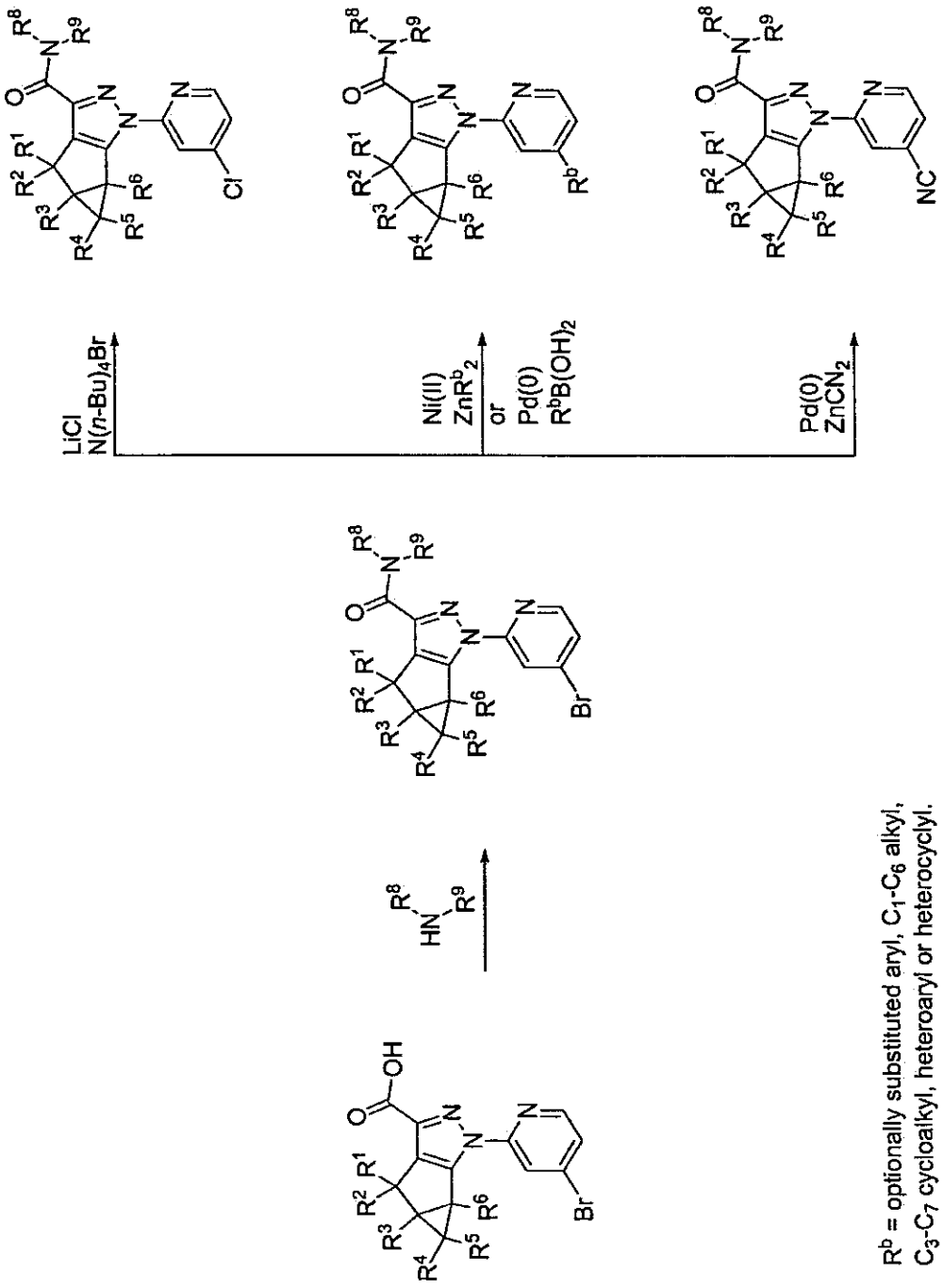

Ni(II)
ZnR$^b_2$
or
Pd(0)
R^{b}B(OH)$_2$
CuCN
NMP
or
Pd(0)
ZnCN$_2$
KF
CuI
CF$_3$Si(Me)$_3$
Z = CH or N
R^b = optionally substituted aryl, C$_1$-C$_6$ alkyl,
C$_3$-C$_7$ cycloalkyl, heteroaryl or heterocyclyl.

Figure 12



R^b = optionally substituted aryl, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, heteroaryl or heterocyclyl.

Figure 13

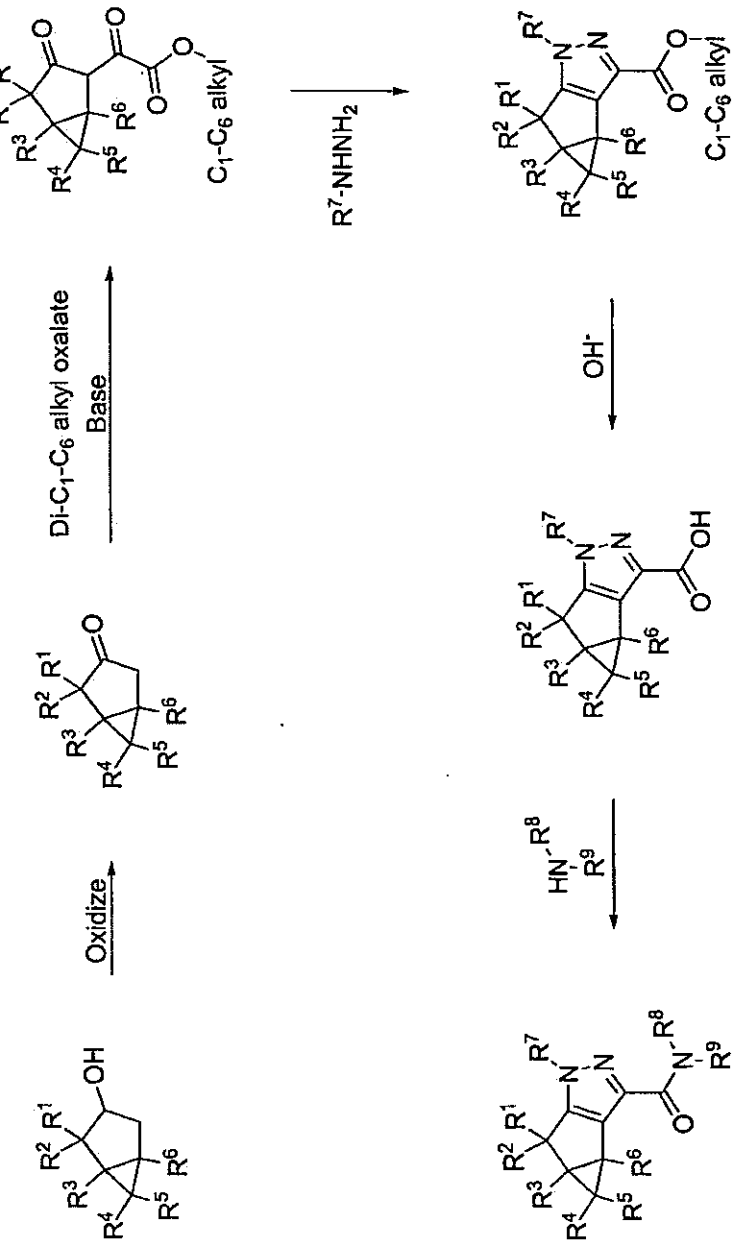

Oxidize
Di-C1-C6 alkyl oxalate
Base
R7-NHNH2
OH-
HN-R8
R9
C1-C6 alkyl

Figure 14

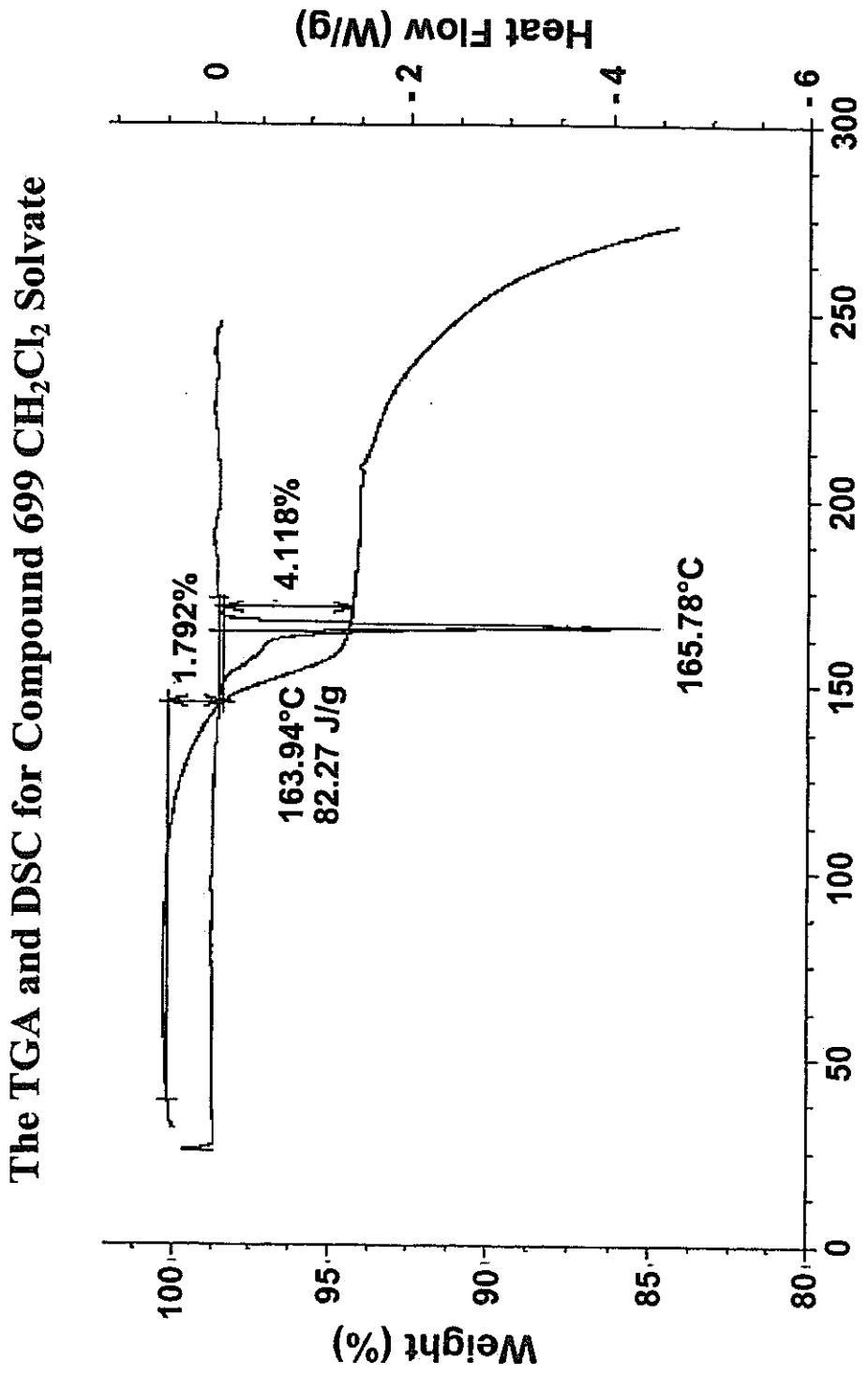

The TGA and DSC for Compound 699 CH_2Cl_2 Solvate
Weight (%)
100
95
90
85
80
Heat Flow (W/g)
0
- 2
- 4
- 6
0
50
100
150
200
250
300
Temperature (°C)
1.792%
4.118%
163.94°C
82.27 J/g
165.78°C

Figure 15

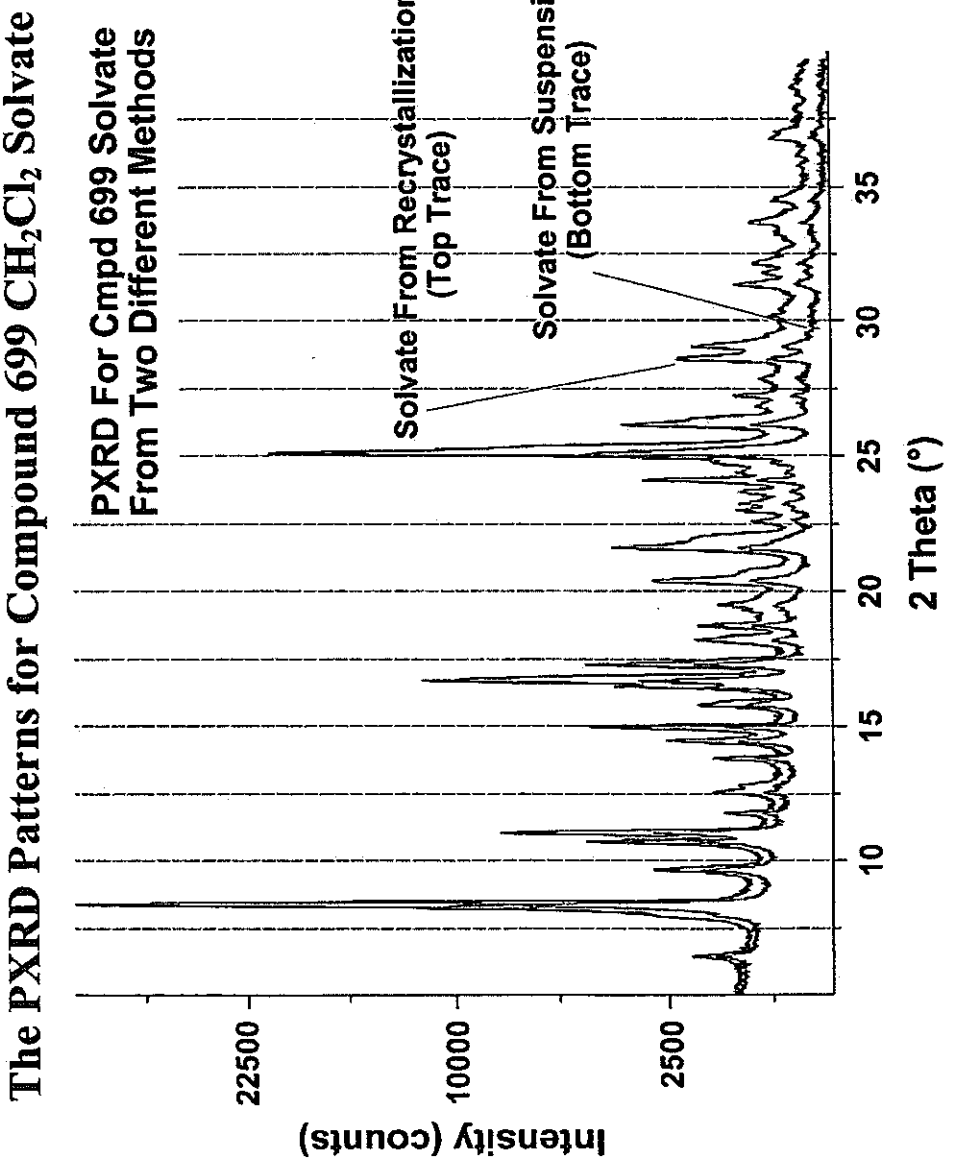

The PXRD Patterns for Compound 699 CH_2Cl_2 Solvate
PXRD For Cmpd 699 Solvate
From Two Different Methods
Solvate From Recrystallization
(Top Trace)
Solvate From Suspension
(Bottom Trace)
Intensity (counts)
22500
10000
2500
10
15
20
25
30
35
2 Theta (°)

Figure 16

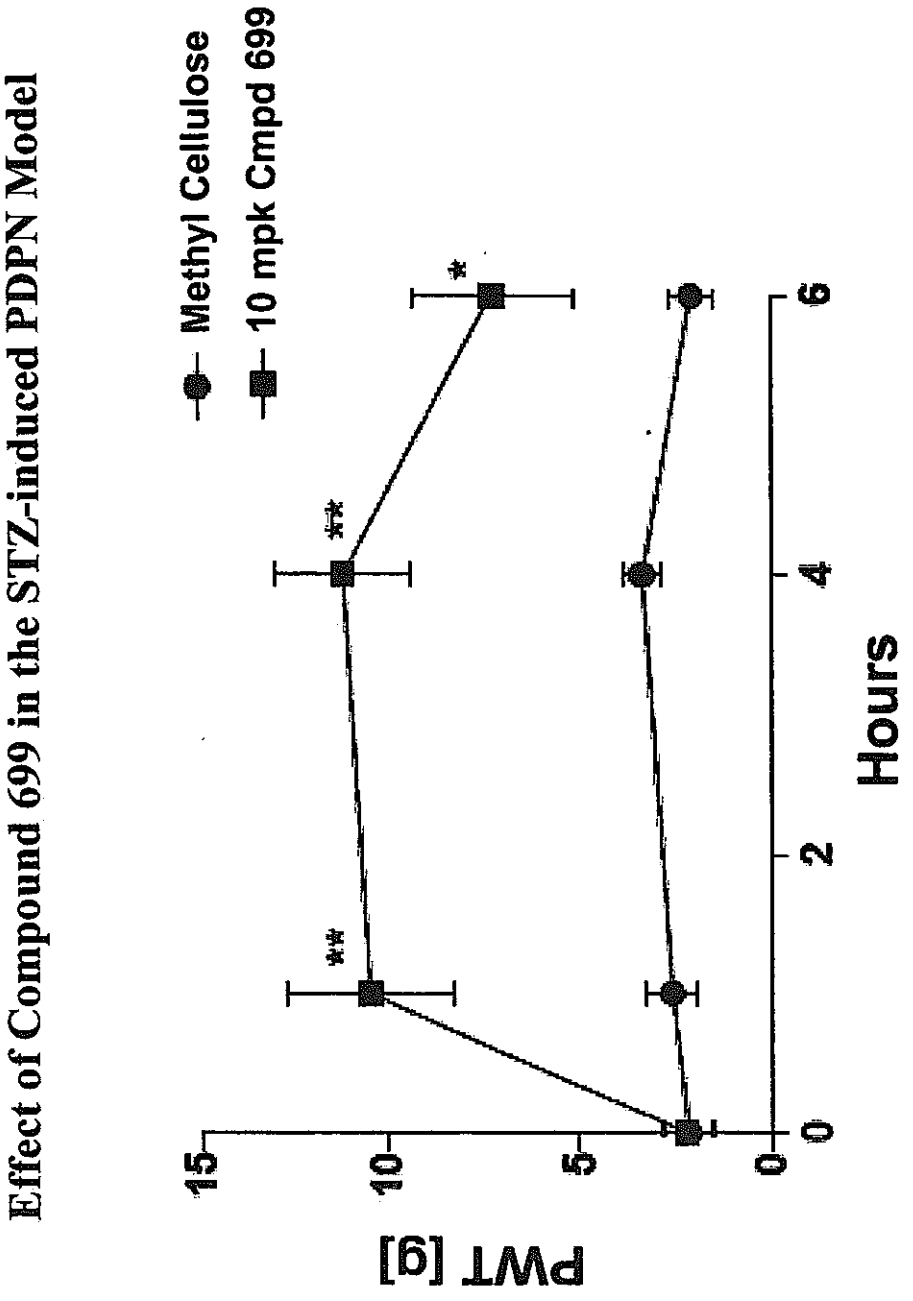

Effect of Compound 699 in the STZ-induced PDPN Model
Methyl Cellulose
10 mpk Cmpd 699
PWT [g]
15
10
5
0
0
2
4
6
Hours
**
**
*

Figure 17

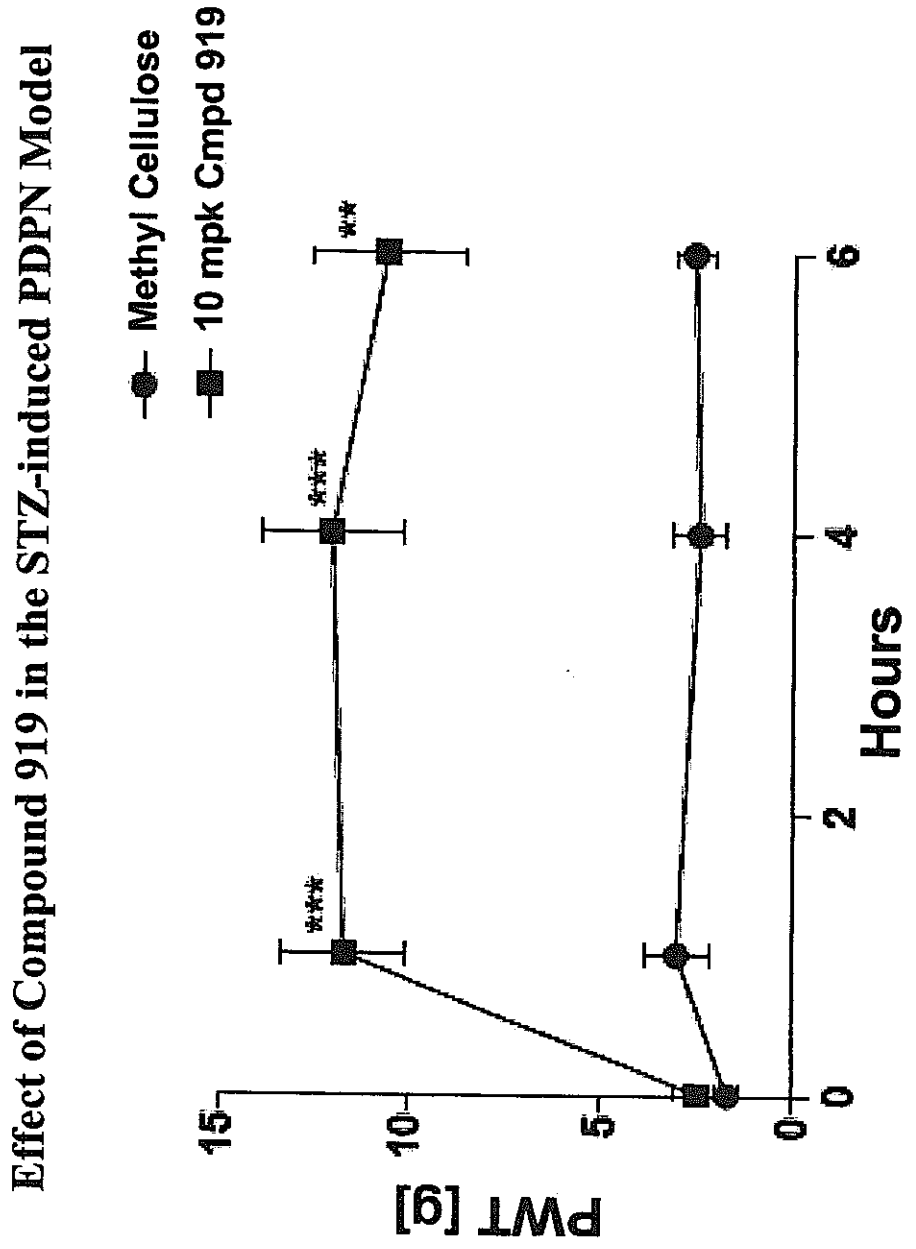

Effect of Compound 919 in the STZ-induced PDPN Model
Methyl Cellulose
10 mpk Cmpd 919
PWT [g]
15
10
5
0
0
2
4
6
Hours
***
***
**

Figure 18