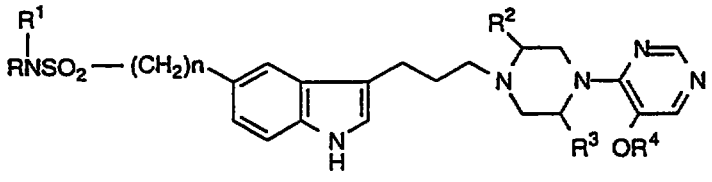
Claims

1. An improved process for preparing certain useful antimigraine agents of Formula (I)



(I)

wherein

R is hydrogen, lower alkyl and trifluoromethyl;

R^1 is hydrogen, lower alkyl and lower alkyl-phenyl;

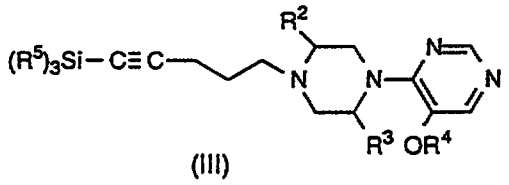
R^2 and R^3 are independently selected from hydrogen and methyl;

R^4 is lower alkyl; and

n is zero or the integers 1 and 2;

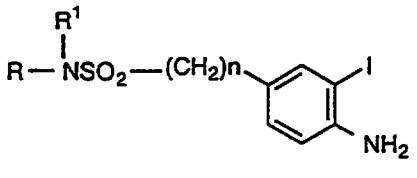
which comprises

a) the reaction of compound (III), wherein R^5 is methyl, ethyl or propyl



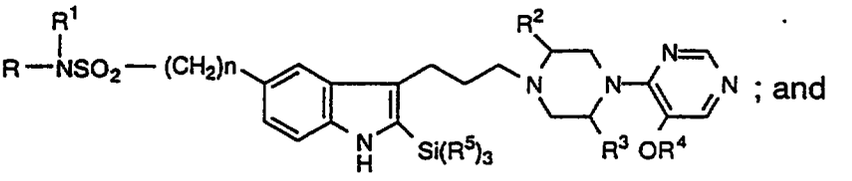
(III)

with compound (IV) in



(IV)

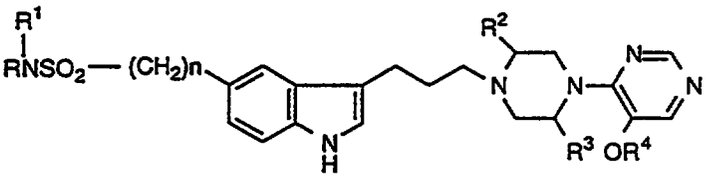
a palladium-catalyzed heteroannulation step to give the 2-$(R^5)_3$Si-indole compound (II)



; and

(II)

b) removal of the trialkylsilyl group of (II) with a mineral acid followed by basification to provide the synthetic product (I)

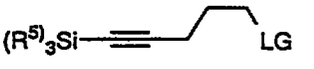


(I)

2. The process of claim 1 wherein R and R^4 are methyl; R^1, R^2 and R^3 are hydrogen and n is 1.

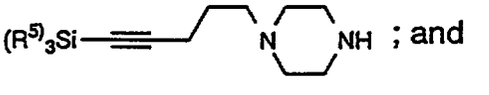
3. The process of claim 1 wherein compound (III) is prepared by

a) the reaction of compound (VIII), wherein LG is a synthetic organic leaving group,



(VIII)

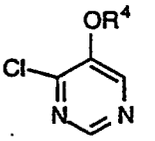
with piperazine to give compound (V)



; and

(V)

b) the reaction of compound (V) with compound (VII)



(VII)

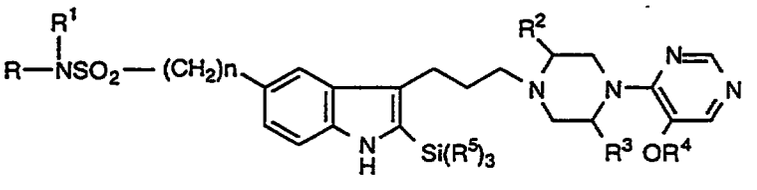
to give compound (III).

4. The process of claims 1 and 3 wherein R^5 is ethyl.

5. The process of claim 1 wherein the heteroannulation of compounds (III) and (IV) is accomplished with palladium acetate, triphenylphosphine, lithium chloride and sodium carbonate in ethanol.

6. The process of claim 1 wherein the 2-$(R^5)_3$Si-indole intermediate of Formula (II) is converted to the product of Formula (I) by treatment with hydrochloric acid to remove the trialkylsilyl moiety.

7. A compound of Formula (II)

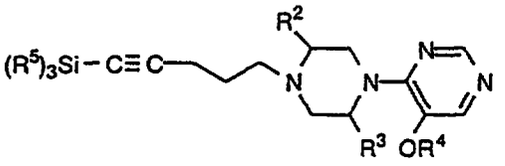


(II)

wherein R is hydrogen, lower alkyl and trifluoromethyl; R^1 is hydrogen, lower alkyl and lower alkyl-phenyl; R^2 and R^3 are independently selected from hydrogen and methyl; R^4 is methyl; R^5 is methyl or ethyl; and n is zero or the integers 1 and 2.

8. The compound of claim 7 wherein R and R^4 are methyl; R^1, R^2 and R^3 are hydrogen; R^5 is ethyl and n is 1.

9. A compound of formula (III)



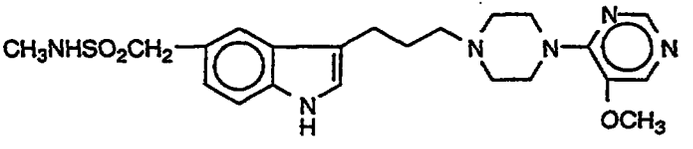
(III)

wherein R^2 and R^3 are independently selected from hydrogen and methyl; R^4 is methyl and R^5 is methyl or ethyl.

10. The compound of claim 9 wherein R^2 and R^3 are hydrogen.

11. The compound of claim 9 wherein R^5 is ethyl.

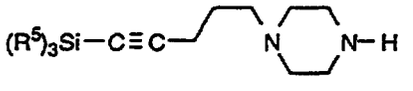
12. An improved process for preparing BMS 180048



BMS 180048

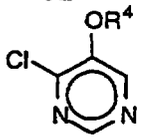
which comprises

a) the reaction of compound (V), wherein R^5 is methyl or ethyl,



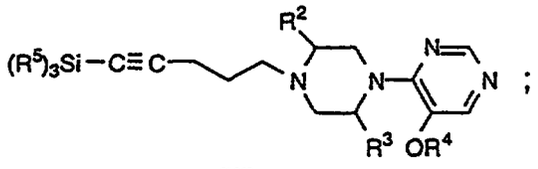
(V)

with compound (VII), wherein R^4 is lower alkyl,



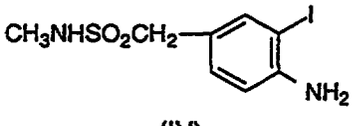
(VII)

to give compound (III)



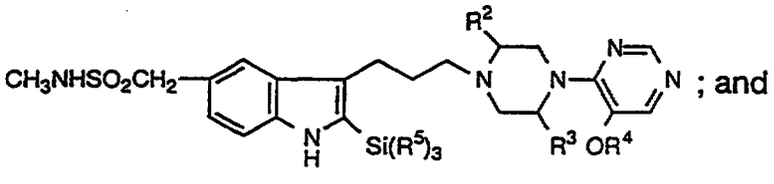
(III)

b) the reaction of compound (III) with compound (IV)



(IV)

in a palladium-catalyzed heteroannulation process to give compound (II)



(II)

c) deprotection of compound (II) with mineral acid to give an acid salt of BMS 180048; and

d) recrystallization of the salt from water followed by basification to provide BMS 180048.

13. The process of claim 12 wherein R^5 is ethyl.