The present invention discloses flinderole compounds/analogs of formula I and to a process for the preparation of same, comprising stereo- and regioselective [3+2] cycloaddition reaction of a tertiary alcohol (la') and a sulphonated diene (lb') in presence of Lewis acid selected from Cu(OTf)2 or BF3OEt2 and a non-polar solvent at room temperature. The flinderole compounds/analogs of the instant invention and prepared by the process described herein is represented by the general formula I, wherein R1-R4 are described herein in the specification.
FLINDEROLE ANALOGUES AND PROCESS FOR SYNTHESIS THEREOF

FIELD OF THE INVENTION

The present invention provides a compound of general formula I and analogues thereof. Particularly, the present invention further discloses a highly stereo- and regioselective \([3+2]\) cycloaddition process for the preparation of Flinderole compound/analogues of general formula I.

The present invention further provides compounds of general formula I which are useful as antimalarial compounds.

BACKGROUND AND PRIOR ART OF THE INVENTION

Malaria is a mosquito-borne infectious disease of humans and other animals caused by eukaryotic protists of the genus Plasmodium. Four strains of the parasite are responsible for malaria in humans, Plasmodium falciparum, P. vivax, P. ovale, and P. malariae. There were an estimated 225 million cases of malaria worldwide in 2009. Ninety percent of malaria-related deaths occur in sub-Saharan Africa, with the majority of deaths being young children. Plasmodium falciparum, the most severe form of malaria, is responsible for the vast majority of deaths associated with the disease. Malaria is commonly associated with poverty, and can indeed be a cause of poverty and a major hindrance to economic development.

With the continuous threat of evolution and rise of multi drug resistant strains of Plasmodium, particularly P. falciparum, there is a growing need to evolve alternatives to drugs such as Chloroquine, Artemisinin and such like. Research along these lines is being carried out to identify new compounds from various resources including plant, microbiological and synthetic.

To respond to the threat of resistance, structurally and functionally novel antimalarial compounds with new mechanisms of action are needed. There are articles and research papers which address flinderole compounds as antimalarial agents and the process for their synthesis. Nitrogen-containing heterocycles have been used as medicinal compounds for centuries, and form the basis for many common drugs such as Morphine (analgesic), Captopril (treatment of hypertension) and Vincristine (cancer chemotherapy).
The chemical structure of the flinderoles is based on the nitrogen-containing indole ring system; however, these compounds have a novel structure not reported in the literature, due to the attachment of the two indole rings. The flinderoles are related to the borreverine compounds, such as isoborreverine,

References may be made to an article titled "Flinderoles A-C: Antimalarial Bis-indole Alkaloids from Flindersia Species" by Liza S. Fernandez et.al in Org. Lett., 2009, 11 (2), pp 329-332, discloses natural product antimalariais, the novel indole alkaloids flinderole A-C which have selective antimalarial activities with IC50 values between 0.15-1.42 µM. Flinderole A was isolated from the Australian plant Flindersia acuminata and flinderoles B and C from the Papua New Guinean plant F. amboinensis. The article further states that Flinderoles A-C contain an unprecedented rearranged skeleton compared to their related isomers of the borreverine class of compounds.

References may be made to PhD research paper titled "The Total Synthesis of the Antimalarial Natural Products, Flinderoles" discusses a methodology for the total synthesis of the novel bis-indole alkaloid ring-system found in the recently isolated natural products, the flinderoles. The thesis proposes two options for coupling the fragments together (Figure 1); a metathesis reaction between two terminal olefins, or a Wittig reaction between a phosphine and a carbonyl group on the respective fragments.

![Figure 1. Proposed routes for coupling Fragments A and B.](image)

The flinderoles disclosed in the prior art are either isolated from the natural sources which have the limitations in view of environmental, biodiversity issues etc. or are synthesized by lengthy, non-economical processes.
To bridge the gap in the therapy for malaria, and with the information that flinderole, isolated from natural product extract, present new molecular scaffold for antimalarial drug discovery, the inventors proposed to further research into these novel compounds for use as an agent against potent and resistant P. falciparum. Also, with the increasing prevalence of the infection, the inventors have also perceived the need to evolve a synthetic process for such effective compounds, such that the process fulfills the market needs for such effective compounds and also leads to compounds with enhanced bioactivity.

10 **OBJECTS OF THE INVENTION**

The main object of the present invention is to provide flinderole compounds / analogues of general formula I, excluding the proviso which comprises known Flinderoles A, B and C, as effective antimalarials.

The another object of the invention is to provide a feasible, cost effective process for the preparation of Flinderoles and its analogues of general formula I as antimalarials especially for effective treatment against Plasmodium falciparum.

Another object of the invention is to provide a highly stereo- and regioselective [3 +2] cycloaddition process for the preparation of Flinderole compound/ analogues of general formula I.

Yet another object of the present invention is to provide a process for the synthesis of compounds of formula I such that the process is useful for production of commercial quantities of such compounds with improved level of bioactivity.

**SUMMARY OF THE INVENTION**

In an aspect, the present invention provides flinderole compounds / analogues of formula I, excluding the provisos which comprises known Flinderoles A, B and C, as effective antimalarials.
Wherein, R\textsubscript{l} to R5 are described herein below. Flinderole compounds of formula I wherein (i) R\textsubscript{i} is \(-\text{CH}_2\text{CH}_2\text{NHMe}\), R\textsubscript{2} is \(-\text{CH}==\text{Ce}_2\); R\textsubscript{3} is \(-\text{H}\); R\textsubscript{5} is \(-\text{CH}_3\), and (ii) when R\textsubscript{i} is \(-\text{CH}_2\text{CH}_2\text{NMMe}_2\), R\textsubscript{2} is \(-\text{CH}==\text{Me}_2\); R\textsubscript{3} is \(-\text{H}\); R\textsubscript{5} \(-\text{CH}_3\).

Accordingly, present invention provides compounds of general formula

![Diagram](image-url)

**General Formula I**

wherein, R\textsubscript{i} is selected independently from \(-\text{CH}_3\), \(-\text{CH}_2\text{CH}_3\), \(-\text{CH}_2\text{CH}_2\text{CH}_3\), \(-\text{Br}\), \(-\text{Cl}\), \(-\text{F}\), \(-\text{I}\), \(-\text{CH}_2\text{OH}\), \(-\text{CH}_2\text{OCH}_3\), \(-\text{CH}_2\text{OBn}\), \(-\text{CH}_2\text{OCH}_2\text{CH}_3\), \(-\text{CH}_2\text{CH}_2\text{OH}\), \(-\text{CH}_2\text{CH}_2\text{Br}\), \(-\text{CH}_2\text{CH}_2\text{NH}_2\), \(-\text{CH}_2\text{CH}_2\text{NMMe}\), \(-\text{CH}_2\text{CH}_2\text{NMMe}_2\), \(-\text{CH}_2\text{NH}_2\), \(-\text{CH}_2\text{NMMe}\), \(-\text{CH}_2\text{NMMe}_2\), \(-\text{4-Fluorophenyl}\), \(-\text{CO}_2\text{H}\), \(-\text{Ph}\), \(-\text{CH}_2\text{CH}_2\text{NMMe}\), \(-\text{CH}==\text{CMe}_2\), \(-\text{CH}==\text{CEt}_2\), \(-\text{OCH}_3\), \(-\text{OCH}_2\text{CH}_3\), \(-\text{COCH}_3\), \(-\text{OH}\), \(-\text{CHO}\), \(-\text{CONH}_2\), \(-\text{CH}_2\text{CONH}_2\), \(-\text{CH}_2\text{CONMe}_2\), \(-\text{CH}_2\text{CONMe}_2\), \(-\text{CN}\), \(-\text{CH}_2\text{CN}\), \(-\text{CH}_2\text{C}_2\text{H}_2\), \(-\text{CH}_2\text{C}_2\text{Me}_2\), \(-\text{CH}_2\text{C}_2\text{Et}\), \(-\text{2-Nitrovinyl}\), \(-\text{CH}_2==\text{CHC}_2\text{H}\), \(-\text{CH}==\text{CHC}_2\text{Me}\), \(-\text{CH}==\text{CHC}_2\text{Et}\), \(-\text{COC}_2\text{H}\), \(-\text{COCONH}_2\), \(-\text{COCONMe}_2\), \(-\text{COCONMe}_2\), \(-\text{CONHHz}\), \(-\text{CONHNH}_2\), \(-\text{COCONMe}_2\), \(-\text{SH}\), \(-\text{SC}_2\text{H}_3\), \(-\text{SCH}==\text{CH}_2\).
-CH₂CH₂CH₂C₂H₃, -OCOCH₃, -OCOCH₂CH₃, OCOC₂H₃CH₂CH₃, -CH₂C₂O₂CH₂CH₃, -CH₂C₂O₂CH₂CH₃,
-COCH₂Ph, -COCH₂Ph, -COOC₂H₃, -OCO(CH₂)₆Me.

R₃ is selected independently from -CH = CH₂, -CH = CHMe, -CH = CMe₂, -CH = C(C₃H₇)₂, -CH = C(C₂H₅)₂, -CH = C(Pr)₂, -CH = C(Me)₂, -CH = C(Pr), -CH = C(C₂H₅), -CH = C(C₃H₇)₂, -CH = C(C₂H₅), -Ph, -PhCl,

-PhCH₃, -PhOMe, -CH₂Ph, -CH₂PhCH₃, -CH₂PhOMe, -CH(Me)₂, -CH₂CH₃, -C(Me)₃, -C₆H₅,

-CH₂CH = CH₂, -CHMeEt, -CH₂C(Me)₃, -CH₂CH = CH₂, -CCPh.

R₃ is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I,

-CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂,

-CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂₃NMe₂, - (4-Fluorophenyl), -C₆H₄, -

CH₂CH = CH₂, -CH = CMe₂, -CH = CET₂, -OCH₃, 0CH₂CH₃, -OCOC₂H₃, -OH, -CHO, -CONH₂,

-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, -CH₂CH₂CONMe₂,

-CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂C₂H₄, -CH₂C₂Me₂, -CH₂C₂Et, - (2-Nitrovinyl),

-CH₂ = CHC₀₂H₂, -CH = C(Me)₂, -CH = CHC₀₂Et, -CH₂ = CHCH₂, -CH₂ = CH₂, -CH₂ = CHC₀₂H₂,

-CH₂ = CHCH₂, -CH₂ = CH₂, -CH₂ = CH₃, -CONMe₂, -C₂H₅NH₂, -C₂H₅NHMe, -C₂H₅NMe₂, - (4-Fluorophenyl), -C₆H₄, -

SC₂H₅, -SCH = CH₂, -CH₂CH₂CH₂C₂H₃, -OCOC₂H₃, -OCOC₂H₃CH₂CH₃, -CH₂C₂O₂CH₂CH₃,

-CH₂C₂O₂CH₂CH₃, -COCH₂Ph, -COCH₂Ph, -COOC₂H₃, -OCO(CH₂)₆Me.

R₄ is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I,

-CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂,

-CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂₃NMe₂, - (4-Fluorophenyl), -C₆H₄, -

CH₂CH = CH₂, -CH = CMe₂, -CH = CET₂, -OCH₃, 0CH₂CH₃, -OCOC₂H₃, -OH, -CHO, -CONH₂,

-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, -CH₂CH₂CONMe₂,

-CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂C₂H₄, -CH₂C₂Me₂, -CH₂C₂Et, - (2-Nitrovinyl),

-CH₂ = CHC₀₂H₂, -CH = C(Me)₂, -CH = CHC₀₂Et, -CH₂ = CHCH₂, -CH₂ = CH₂, -CH₂ = CHC₀₂H₂,

-CH₂ = CHCH₂, -CH₂ = CH₂, -CH₂ = CH₃, -CONMe₂, -C₂H₅NH₂, -C₂H₅NHMe, -C₂H₅NMe₂, - (4-Fluorophenyl), -C₆H₄, -

SC₂H₅, -SCH = CH₂, -CH₂CH₂CH₂C₂H₃, -OCOC₂H₃, -OCOC₂H₃CH₂CH₃, -CH₂C₂O₂CH₂CH₃,

-CH₂C₂O₂CH₂CH₃, -COCH₂Ph, -COCH₂Ph, -COOC₂H₃, -OCO(CH₂)₆Me.

R₅ is selected independently from -CH₃, -CH = CH₂, -CH = CHMe, -CH = CMe₂, -CH = CET₂, -CH = CET₂, -CH = C(Pr)₂, -CH = C(Pr), -CH = CH(i-Pr), -CH = C(i-Pr), -CH = CHPh, -CH = C(Ph)₂,

-CH = CH(Indole).

With the proviso, when R4 is as indicated herein below,
5 $R_8$ selected from -H, -CH$_3$, -CH$_2$CH$_3$, -CH$_2$CH$_2$CH$_3$, -Br, -Cl, -F, -I, -CH$_2$OH, -CH$_2$OCH$_3$, -CH$_2$OBn, -CH$_2$OCH$_2$CH$_3$, -CH$_2$CH$_2$NH$_2$, -CH$_2$CH$_2$NHMe, -CH$_2$CH$_2$NMe$_2$, -CH$_2$NH$_2$, -CH$_2$NHMe, CH$_2$NMe$_2$, - (4-Fluorophenyl), -CO$_2$H, -Ph, -CH$_2$CH$_2$=CH$_2$, -CH=CHMe, -CH=C$_2$H, -OCH$_3$, OCH$_2$CH$_3$, -OH, -CHO, -CONH$_2$, -CH$_2$CONHMe, -CH$_2$CONMe$_2$, -CH$_2$COCONHMe, -CH$_2$COCONMe$_2$, -CH$_2$CH$_2$CONHMe, -CH$_2$CH$_2$CONMe$_2$, -CN, -CH$_2$CN, -CH$_2$C$_6$H$_5$, -CH$_2$C$_6$H$_4$, -CH$_2$CO$_2$Me, -CH$_2$CO$_2$Et, - (2-Nitrovinyl), -CH$_2$=CHC$_6$H$_5$, -CH=CHC$_6$H$_5$, -CH=CHC$_6$H$_5$, -CH$_2$=CHCN, -COCO$_2$H, -COCONH$_2$, -COCONMe$_2$, -CH$_2$CH$_2$CO$_2$H, -CONH$_2$, -CONHMe, -CH$_2$CH$_2$CONMe$_2$, -SH, -SC$_2$H$_5$, -SC=CH$_2$, -CH$_2$CONH$_2$, -CH$_2$CONMe$_2$, -CH$_2$CONNH$_2$, -COCONMe$_2$, -CH$_2$CONMe$_2$, -COOCH$_2$CH$_3$, -OCOCH$_2$CH$_2$CH$_3$, -CH$_2$CO$_2$C$_6$H$_5$, -CH$_2$C$_6$H$_5$, -CH$_2$CO$_2$Ph, -COCH$_2$Ph, -COCOCl, -OCO(CH$_2$)$_6$Me;

10 with the provisio, when

15 $R_7$ represents -H, -CH$_3$, -COCH$_3$, -S02Ph, -(BOC), -(Ph-F), -(Bn), -(C$_3$H$_7$F), -(CO$_2$Et), -(MOM);

$R_8$ represents -H, -CH$_3$, -CH$_2$CH$_3$, -CH$_2$CH$_2$CH$_3$, -Br, -Cl, -F, -I, -CH$_2$OH, -CH$_2$OCH$_3$, -CH$_2$OBn, -CH$_2$OCH$_2$CH$_3$, -CH$_2$CH$_2$NH$_2$, -CH$_2$CH$_2$NHMe, -CH$_2$CH$_2$NMe$_2$, -CH$_2$NH$_2$, -CH$_2$NHMe, CH$_2$NMe$_2$, - (4-Fluorophenyl), -CO$_2$H, -Ph, -CH$_2$CH$_2$=CH$_2$, -CH=CHMe, -CH=C$_2$H, -OCH$_3$, OCH$_2$CH$_3$, -OH, -CHO, -CONH$_2$, -CH$_2$CONHMe, -CH$_2$CONMe$_2$, -CH$_2$COCONHMe, -CH$_2$COCONMe$_2$, -CH$_2$CH$_2$CONHMe, -CH$_2$CH$_2$CONMe$_2$, -CN, -CH$_2$CN, -CH$_2$C$_6$H$_5$, -CH$_2$C$_6$H$_4$, -CH$_2$CO$_2$Me, -CH$_2$CO$_2$Et, - (2-Nitrovinyl), -CH$_2$=CHC$_6$H$_5$, -CH=CHC$_6$H$_5$, -CH=CHC$_6$H$_5$, -CH$_2$=CHCN, -COCO$_2$H, -COCONH$_2$, -COCONMe$_2$, -CH$_2$CH$_2$CO$_2$H, -CONH$_2$, -CONHMe, -CH$_2$CH$_2$CONMe$_2$, -SH, -SC$_2$H$_5$, -SC=CH$_2$, -CH$_2$CONH$_2$, -CH$_2$CONMe$_2$, -CH$_2$CONNH$_2$, -COCONMe$_2$, -CH$_2$CONMe$_2$, -COOCH$_2$CH$_3$, -OCOCH$_2$CH$_2$CH$_3$, -CH$_2$CO$_2$C$_6$H$_5$, -CH$_2$C$_6$H$_5$, -CH$_2$CO$_2$Ph, -COCH$_2$Ph, -COCOCl, -OCO(CH$_2$)$_6$Me;

20 $R_9$ represents -H, -CH$_3$, -CH$_2$CH$_3$, -CH$_2$CH$_2$CH$_3$, -Br, -Cl, -F, -I, -CH$_2$OH, -CH$_2$OCH$_3$, -CH$_2$OBn, -CH$_2$OCH$_2$CH$_3$, -CH$_2$CH$_2$NH$_2$, -CH$_2$CH$_2$NHMe, -CH$_2$CH$_2$NMe$_2$, -CH$_2$NH$_2$, -CH$_2$NHMe, CH$_2$NMe$_2$, - (4-Fluorophenyl), -CO$_2$H, -Ph, -CH$_2$CH$_2$=CH$_2$, -CH=CHMe, -CH=C$_2$H, -OCH$_3$, OCH$_2$CH$_3$, -OH, -CHO, -CONH$_2$, -CH$_2$CONHMe, -CH$_2$CONMe$_2$, -CH$_2$COCONHMe, -CH$_2$COCONMe$_2$, -CH$_2$CH$_2$CONHMe, -CH$_2$CH$_2$CONMe$_2$, -CN, -CH$_2$CN, -CH$_2$C$_6$H$_5$, -CH$_2$C$_6$H$_4$, -CH$_2$CO$_2$Me, -CH$_2$CO$_2$Et, - (2-Nitrovinyl), -CH$_2$=CHC$_6$H$_5$, -CH=CHC$_6$H$_5$, -CH=CHC$_6$H$_5$, -CH$_2$=CHCN, -COCO$_2$H, -COCONH$_2$, -COCONMe$_2$, -CH$_2$CH$_2$CO$_2$H, -CONH$_2$, -CONHMe, -CH$_2$CH$_2$CONMe$_2$, -SH, -SC$_2$H$_5$, -SC=CH$_2$, -CH$_2$CONH$_2$, -CH$_2$CONMe$_2$, -CH$_2$CONNH$_2$, -COCONMe$_2$, -CH$_2$CONMe$_2$, -COOCH$_2$CH$_3$, -OCOCH$_2$CH$_2$CH$_3$, -CH$_2$CO$_2$C$_6$H$_5$, -CH$_2$C$_6$H$_5$, -CH$_2$CO$_2$Ph, -COCH$_2$Ph, -COCOCl, -OCO(CH$_2$)$_6$Me;

25 $R_9$ represents -H, -CH$_3$, -CH$_2$CH$_3$, -CH$_2$CH$_2$CH$_3$, -Br, -Cl, -F, -I, -CH$_2$OH, -CH$_2$OCH$_3$, -CH$_2$OBn,
-OCH₃, OCH₂CH₃, -COCH₃, -OH, -CHO, -CONH₂, -CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H, -CH₂CO₂Me, -CH₃CO₂Et, -2-Nitrovinyl, -CH₂=CHCO₂H, -CH=CHCO₂Me, -CH=CHCO₂Et, -CH₂=CHCN, -CO₂H, -COCONH₂, -COCONMe₂, -CH₂CH₂CO₂H, -CONNH₂, -CH₂CONNH₂, -COCONMe₂, -SH, -SC₂H₅, -SCH=CH₂, -CH₂CH₂CH₂CO₂H, -OCOCH₃, -OCOCH₂CH₃, -CH₂CO₂CH₂CH₃, -COCH₂Ph, -COCH₂Ph, -COCOCI, -OCO(CH₂)₆Me.

With the proviso, when R₄ is as indicated herein below.

\[ R₄ = \]

10 R₆ represents -H, -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₃NH₂, -CH₂NHMe, CH₂NMe₂, -(4-Fluorophenyl), -C₆H₄H, -Ph, -CH₂CH=CH₂, -CH=CH₂, -CH=CEt₂, -OCH₃, OCH₂CH₃, -COCH₃, -OH, -CHO, -CONH₂, -CH₂CONH₂, -CH₂CONMe₂, -CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONMe₂, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H, -CH₂CO₂Me, -CH₂CO₂Et, -CH₂=CHCN, -CO₂H, -COCONH₂, -COCONMe₂, -CH₂CH₂CO₂H, -CONNH₂, -CH₂CONNH₂, -COCONMe₂, -SH, -SC₂H₅, -SCH=CH₂, -CH₂CH₂CH₂CO₂H, -OCOCH₃, -OCOCH₂CH₃, -CH₂CO₂CH₂CH₃, -COCH₂Ph, -COCH₂Ph, -COCOCI, -OCO(CH₂)₆Me.

15 -CH₂CO₂Et, -2-Nitrovinyl, -CH₂=CHCO₂H, -CH=CHCO₂Me, -CH=CHCO₂Et, -CH₂=CHCN, -CO₂H, -COCONH₂, -COCONMe₂, -CH₂CH₂CO₂H, -CONNH₂, -CH₂CONNH₂, -COCONMe₂, -SH, -SC₂H₅, -SCH=CH₂, -CH₂CH₂CH₂CO₂H, -OCOCH₃, -OCOCH₂CH₃, -CH₂CO₂CH₂CH₃, -COCH₂Ph, -COCH₂Ph, -COCOCI, -OCO(CH₂)₆Me.

20 R₇ = -H, -CH₃, -COCH₃, -SO₂Ph, -(BOC), -(PhF), -(Bn), -(C₅H₁₀F), -(C₂H₅), -(MOM).

With the proviso, when

\[ R₄ = \]

R₆ represents -H, -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₃NH₂, -CH₂NHMe, CH₂NMe₂, -(4-Fluorophenyl), -C₆H₄H, -Ph, -CH₂CH=CH₂, -CH=CH₂, -CH=CEt₂, -OCH₃, OCH₂CH₃, -COCH₃, -OH, -CHO, -CONH₂, -CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂NHMe, CH₂NMe₂, -(4-Fluorophenyl), -C₆H₄H, -Ph, -CH₂CH=CH₂, -CH=CH₂, -CH=CEt₂, -OCH₃, OCH₂CH₃, -COCH₃, -OH, -CHO, -CONH₂, -CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂,
the preparation of Flinderole A-C and compounds of general formula I as claimed in claim 1 comprising the steps of:

\[
\text{R}_1, \text{R}_2, \text{R}_3, \text{R}_4, \text{R}_5, \text{R}_6, \text{R}_7
\]

with the proviso, when \( \text{R}_1 \) is \(-\text{CH}_2\text{CH}_2\text{NHMe} \), \( \text{R}_2 \) is \(-\text{CH}=\text{CMe}_2 \), \( \text{R}_3 \) is \(-\text{H} \), \( \text{R}_5 \) is \(......\text{CH}_3 \),

\[
\text{R}_4 = \begin{array}{c}
\text{N} \\
\text{R}_6 \\
\text{R}_7
\end{array}
\]

\( \text{R}_5 \) is \(-\text{CH}_2\text{CH}_2\text{NHMe} \) and \( \text{R}_7 \) is \(-\text{H} \);

with the proviso, when \( \text{R}_1 \) is \(-\text{CH}_2\text{CH}_2\text{NMe}_2 \), \( \text{R}_2 \) is \(-\text{CH}=\text{CMe}_2 \), \( \text{R}_3 \) is \(-\text{H} \), \( \text{R}_5 \) \(-\text{CH}_3 \),

\[
\text{R}_4 = \begin{array}{c}
\text{N} \\
\text{R}_6 \\
\text{R}_7
\end{array}
\]

\( \text{R}_6 \) is \(-\text{CH}_2\text{CH}_2\text{NMe}_2 \) and \( \text{R}_7 \) is \(-\text{H} \) are excluded.

In an embodiment of the present invention, said compounds are useful as anti-malarial compound.
a. reacting indole aldehyde (lc') with Ph3P=CHC02Et followed by reaction of the resultant ester with MeMgBr to obtain tertiary alcohol (ld');

\[
\text{R}_1' \text{CHO} \quad \text{R}_2' \text{SO}_2 \text{Ph}
\]

\[
\text{R}_1' \text{CHO} \quad \text{R}_2' \text{SO}_2 \text{Ph} \quad \text{OH} \quad \text{R}_3'
\]

b. mesylating tertiary alcohol (ld') as obtained in step (a) followed by elimination to obtain sulphonated diene (lb');

\[
\text{R}_1' \text{R} \quad \text{SO}_2 \text{Ph}
\]

\[
\text{R}_1' \text{R} \quad \text{SO}_2 \text{Ph} \quad \text{R}_4
\]

c. desulfonylating (lb') as obtained in step (b) using methanolic NaOH to obtain desulphonated diene (le');

\[
\text{R}_1' \text{R} \quad \text{R}_4
\]

\[
\text{R}_1' \text{R} \quad \text{R}_4 \quad \text{R} = \text{H}
\]

d. desulfonylating alcohol (ld') as obtained in step (a) with sodium amalgam to obtain alcohol (la'); and

\[
\text{R}_1' \text{R} \quad \text{R}_2' \quad \text{OH} \quad \text{R}_3'
\]

\[
\text{R}_1' \text{R} \quad \text{R}_2' \quad \text{OH} \quad \text{R}_3'
\]

e. reacting alcohol (la') as obtained in step (d) optionally with sulphonated diene
(lb') as obtained in step (b) or desulphonated diene (le') as obtained in step (c) in presence of Lewis acid and a non-polar solvent at temperature in the range of 25 to 32°C to obtain sulphonated or desuphonated compound of general formula 1;
f. desulfonylating sulphonated compound of general formula 1 as obtained in step (e) using methanoic NaOH to obtain desulphonated Flinderole A-C and compounds of general formula 1.

In yet another embodiment of the present invention, Lewis acid used in step (e) is selected from Cu(OTf)2 or B(OPh)3 OEt.

In yet another embodiment of the present invention, the process for the preparation of compounds of general formula I, optionally comprising dimerization of alcohol (la') and the said process comprising the steps of:

a. adding alcohol (la') with lewis acid with stirring for a period in the range of 50 to 70 minutes at temperature in the range of 25 to 32°C followed by adding water to obtain reaction mixture;
b. extracting the reaction mixture as obtained in step (a) with non-polar solvent, washing with brine, drying followed by evaporating the solvent;
c. purifying the residue on silica gel column using EtOAc-hexane (1:39) to obtain compound of general formula 1.

In yet another embodiment of the present invention, Lewis acid used in step (a) is selected from Cu(OTf)2 or B(OPh)3 OEt.

In yet another embodiment of the present invention, a pharmaceutical composition for
the treatment of malaria comprising compounds of general formula I optionally along with pharmaceutically acceptable excipients.

**BRIEF DESCRIPTION OF THE FIGURES**

Scheme 1 represents the cycloaddition reaction between a tertiary alcohol (la') and an olefin (lb') to obtain compound of general formula 1.

Scheme 2 represents the structures of flnderoles A-C and the proposed biosynthetic pathway.

Scheme 3 represents flow chart for the preparation of compound of general formula 1.

Scheme 4 represents process steps for the preparation of intermediate compounds.

Scheme 5 represents compound 11 to 17 and process steps for the preparation of compound 9a, 9b, 10a and 10b.

Scheme 6 represents process steps for the preparation of compound 17-28 and flnderole B and C.

Figure 1' represents proposed stereo chemical model for the [3+2] cycloaddition.

**DETAILED DESCRIPTION OF INVENTION**

The present invention provides Flnderole compounds/ analogues of general formula I, 

\[
\begin{array}{c}
\text{R}_1 \\
\text{R}_2 \\
\text{R}_3 \\
\text{R}_4 \\
\text{R}_5 \\
\end{array}
\]

General formula 1

The present invention also relates to a highly stereo- and regioselective [3 +2] cycloaddition reaction between a tertiary alcohol (la') and a diene (lb') (olefin) in presence of Lewis acid and a non-polar solvent at room temperature (25 to 32°C). (Scheme 1).

In an aspect, the process for the preparation of flnderoles of compounds/ analogues of formula I by the instnsnt invention includes Flnderoles A, B and C.

Flnderoles A, B and C contain an unprecedented rearranged skeleton compared to their related isomers of the borreverine class of compounds. (Scheme 2)

Symmetrical retrosynthetic analysis of the dimeric structure of flnderoles revealed monomeric tryptamine diene as a possible precursor for the synthesis of flnderoles.
Exploration of the biosynthetic pathway as shown in Scheme 1 above lead to the conclusion that diene might undergo dimerization leading to the flinderole framework. The diene (le') is prepared from the known indole aldehyde (lc') (Scheme 3). Treatment of indole aldehyde (lc') with Ph3P=CHC02Et followed by reaction of the resultant ester with MeMgBr generated the tertiary alcohol (la'). Mesylation of alcohol (la') and subsequent elimination yielded diene (lb'), which give the required diene (le') upon desulfonylation using methanolic NaOH. The diene (le') is found to polymerize with different Lewis acids under various reaction conditions employed, resulting in intractable mixtures. It is reasonably concluded that the actual site of protonation in 4 is at C3 of the indole nucleus to produce a conjugated enamine, which could undergo cationic polymerization.

At this juncture, it was reasoned that if diene (le') is generated in situ in sufficiently low concentration, it might undergo dimerization by a formal intermolecular [3+2] cycloaddition, leading to the flinderole framework. Accordingly, the available alcohol (ld') is desulfonylated to obtain alcohol (la') as shown in Scheme 3.

The present invention discloses the preparation of flinderoles 9a and 9b by dimerization of alcohol (8) in presence of various Lewis acids as shown in Scheme 4 and Table 1 below. Various Lewis acids were screened for the proposed dimerization of the alcohol 8 and results are summarized in Table 1.

**Table 1:** Invention and optimization of dimerization reaction of the alcohol (8)

<table>
<thead>
<tr>
<th>entry</th>
<th>Lewis acid</th>
<th>Yield (%)</th>
<th>dr (9a:9b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TMSOTf</td>
<td>10</td>
<td>1:1</td>
</tr>
<tr>
<td>2</td>
<td>Yb(OTf)</td>
<td>25</td>
<td>1:1</td>
</tr>
<tr>
<td>3</td>
<td>Sc(OTf)</td>
<td>25</td>
<td>1:1</td>
</tr>
<tr>
<td>4</td>
<td>BF3-OEt</td>
<td>38</td>
<td>3:2</td>
</tr>
<tr>
<td>5</td>
<td>Cu(OTf)</td>
<td>46</td>
<td>2:1</td>
</tr>
<tr>
<td>6</td>
<td>CF3CO2H</td>
<td>35</td>
<td>3:2</td>
</tr>
<tr>
<td>7</td>
<td>Tf2O</td>
<td>0</td>
<td>N.A.</td>
</tr>
</tbody>
</table>
Reaction of the alcohol (8) with TMSOTf furnished a complex mixture of products and the dimers (9a, b) were obtained in poor yield as 1:1 mixture of diastereomers (Table 1, entry 1). Similarly, Yb(OTf)₃ and Sc(OTf)₃ gave the desired adducts (9a, b) in low yield (Table 1, entries 2 and 3). BF₃·OEt₂ was found to be useful catalyst for effecting this transformation in much cleaner manner generating the products (9a, b) albeit in moderate yield and diastereoselectivity (Table 1, entry 4). Even though Tf₂O did not give any desired product, trifluoroacetic acid did furnish the required product (9a, b) in comparable yield (Table 1, entries 6 and 7). More interestingly Cu(OTf)₂ generated the framework 9a and 9b in much improved yield and diastereoselectivity (Table 1, entry 5). The dimers 9a and 9b could be separated by careful column chromatography and their structures were established by spectroscopic analysis (¹H, ¹³C, IR, HRMS) and with the comparison of spectral data. Their relative stereochemistry was determined by ROESY.

The scope of the dimerization reaction discussed above was further extended to reaction between the intermediate generated in situ of alcohol(la') and the diene (lb') bearing a sulfonyl group in presence of Cu(OTf)₂ to obtain flinderoles in good yield and diastereoselectivity. (Figure 1)

The present invention provides a highly stereo- and regioselective [3 +2] cycloaddition reaction between a tertiary alcohol (la') and a sulphonated diene (lb') in presence of Lewis acid selected from Cu(OTf)₂ or BF₃·OEt₂ for the synthesis of flinderole compounds and its analogues of formula 1 comprising:

2. reacting indole aldehyde (la') with Ph3P=CHC02Et followed by reaction of the resultant ester with MeMgBr to obtain tertiary alcohol (Id');
3. mesylating alcohol (Id') followed by elimination to yield sulphonated diene (lb');
4. desulfonylating (lb') using methanolic NaOH to obtain diene (le');
5. desulfonylating alcohol (Id') to obtain alcohol(la'); and
6. reacting alcohol (la') with sulphonated diene (lb') in presence of Lewis acid Cu(OTf)₂ and a nono polar solvent at room temperature to obtain desired compounds of formula 1.

The processes for the preparation of various Flinderoles are described in Scheme 5 and Scheme 6.

Scheme 5 describes the dimerization reaction. Tert-alcohol 8 and the diene 7 are mixed together and treated with Cu(OTf)₂, the dimers 10a, b are obtained in requisite yield and
diastereoselectivity (>19:1). When BF₃·OEt₂ is used as catalyst, diastereomeric ratio drops to 2:1. Reaction is found to work with equal efficiency when tert-alcohol had ethyl rather than methyl substitution (cf. the adduct 11). Similarly, having an ethoxymethyl substituent on the C3 of indole did not affect the yield or selectivity (cf. the adducts 12 and 13).

According to Scheme 6, primary hydroxyl group of the compound 20 is acylated using acetic anhydride to furnish the aceta 21. Formylation of the acetate 21 using dichloromethyl methyl ether and stannic chloride gave the acetate 22. The acetyl protection in the indole derivative 22 is changed to TBS-protection following hydrolysis of acetate and reaction of the resultant alcohol with TBSCI to obtain TBS-ether 23. Wittig olefination of the aldehyde 23 with Ph₃P=CHC₂₂Et generated the unsaturated ester in 91% yield, which on treatment with methyl magnesium iodide give tertiary alcohol 24. Dehydration of the hydroxyl group of alcohol 24 is achieved via its mesylate followed by elimination to furnish the requisite olefin 19. Deprotection of the phenylsulfonyl group in alcohol 24 with sodium amalgam gives the other coupling partner, alcohol 18 (Scheme 6).

An equimolar mixture of the tert alcohol 18 and the diene 19 are treated with catalytic amount of copper(II) triflate, which lead to the adduct 25a in 62% yield with diastereoselectivity. Surprisingly, when a mixture of the tert-alcohol 18 and the diene 19 is treated with excess of BF₃·OEt₂, not only it gives the expected dimerization product but also deprotected both TBDMS groups to directly generate the diols 26a,b. The major compound is found to be the isomer 26a in which the methyl and isobutylene groups are cis to each other. Oxidation of the mixture of the diols 26a,b using IBX followed by reductive amination of the resultant bisaldehydes 27a,b give a mixture of the amines 28a,b in 91% yield. Deprotection of indole nitrogen of 28a,b followed by purification by preparative TLC delivers flinderole B (2) and flinderole C (3), which is treated individually with 0.005M TFA in acetonitrile to get the TFA salt of flinderoles B and C. The TFA salt of synthetic flinderoles B and C thus obtained possess physical properties (IR, mass, ¹H, ¹³C) identical to those reported in the literature.

Compounds of formula 9a and 9b are obtained by dimerization of alcohol (8). According to the process, to a solution of the alcohol 8 in anhydrous CH₂Cl₂ is added a catalytic amount of Cu(OTf)₂ and stirred magnetically for 1 h at RT. The progress of reaction is
monitored by TLC till the starting alcohol had been completely consumed. Water is added
to the reaction mixture, extracted with CH₂Cl₂, washed with brine and dried over Na₂SO₄.
The solvent is evaporated followed by purification of the residue on silica gel column
using EtOAc-hexane (1:39) as eluent to furnish isomer 9a. Further, elution of the column
with EtOAc-hexane (1:39) yield isomer 9b as white crystalline solid.

In yet another embodiment, compound of formula 9a and 9b are obtained by
desulphonation of compounds of formula 10a and 10b using sodium amalgam
as shown in Scheme 6.

The flinderole compounds/analogues of formula I finds use in pharmaceutical industry, in
agriculture; preferably in pharmaceutical industry for the treatment of malaria especially
against Plasmodium falciparum.

The present invention provides a method of treatment or prevention of malaria to a
subject by administering an effective amount of the compound of Formula I along with
one or more suitable pharmaceutical carriers/excipients. The dosage forms include solid
dosage forms such as tablets, powders, capsules, liquid dosage forms as well as
parenteral dosage forms. The dosage forms can also be prepared as sustained,
controlled, modified and immediate release dosage forms. Active ingredient(s) and
excipients can be formulated into compositions and dosage forms according to methods
known in the art.

In summary, a highly stereo- and regioselective formal [3+2] cycloaddition reaction
between a tertiary alcohol (la') and sulphonated olefin(lb') has been developed for use
in the synthesis of pyrrolo[1,2-a] indoles, i.e Flinderole compounds/ analogues of formula
I. The potential of this methodology has been amply demonstrated in the first total
synthesis of the isomeric flinderoles B and C, which involves 11 steps in the longest linear
sequence and gave an overall yield of 17.2%. The strategy is fairly general and is
amenable to the synthesis of other natural products of this class as well as their
analogues.

Examples
Following examples are given by way of illustration therefore should not be
construed to limit the scope of the invention.

All reactions were carried out under nitrogen atmosphere with dry solvents under
anhydrous conditions, unless otherwise mentioned. All the chemicals were purchased commercially, and used without further purification. Anhydrous THF and diethyl ether were distilled from sodium-benzophenone, and dichloromethane was distilled from calcium hydride. Yields refer to chromatographically pure material, unless otherwise stated.

Reaction were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel plates (60F-254) using UV light as a visualizing agent and an p-anisaldehyde or ninhydrine stain, and heat as developing agents. Merck silica gel (particle size 100-200 and 230-400 mesh) was used for flash column chromatography.

Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. NMR spectra were recorded on either a Bruker Avance 200 ($^1$H: 200 MHz, $^{13}$C: 50MHz), Bruker Avance 400 ($^1$H : 400 MHz, $^{13}$C: 100MHz), Bruker Avance 500 ($^1$H: 500 MHz, $^{13}$C: 125 MHz). Mass spectrometric data were obtained using QTOF-Micromass-UK.

The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, ddd = doublet of a doublet of a doublet, dt = doublet of a triplet, m = multiplet, br = broad.

Example 1

Synthesis of compound 9a and 9b

\[
\begin{align*}
\text{Cu(OTf)}_2 \text{CH}_2\text{Cl}_2 & \xrightarrow{\text{RT, 1h, 46\%}} \text{9a, 31\%} \\
\text{9b, 15\%}
\end{align*}
\]

solution of the alcohol 8 (50 mg, 0.23 mmol) in anhydrous CH$_2$Cl$_2$ (6 ml) was added a catalytic amount of Cu(OTf)$_2$ (15 mg, 0.04 mmol) and stirred magnetically for 1 h at RT. The progress of reaction was monitored by TLC till the starting alcohol has been completely consumed. Water (5 ml) was added to the reaction mixture, extracted with CH$_2$Cl$_2$ (3 x 5 ml), washed with brine (5 ml) and dried over Na$_2$SO$_4$. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:39) as
eluent furnished the isomer 9a (28 mg, 31%) as white crystalline solid; Rf = 0.5 (EtOAc-hexane 1:19);

IR (neat): \( \nu_{max}/cm^{-1} \) 3362, 3053, 2926, 1697, 1454, 1377, 789, 457; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 7.91 (br s, 1H), 7.60-6.95 (m, 8H), 6.80 (d, \( J = 16.6 \) Hz, 1H), 6.23 (d, \( J = 16.3 \) Hz, 1H), 5.27 (d, \( J = 9.3 \) Hz, 1H), 4.24 (q, \( J = 17.3 \) Hz, 1H), 2.69-2.60 (m, 1H), 2.41-2.30 (m, 4H), 2.20 (s, 3H), 1.82 (d, \( J = 16 \) Hz, 6H), 1.72 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 142.0, 136.2, 133.7, 133.1, 132.0, 131.2, 131.1, 129.9, 124.9, 123.1, 120.2, 119.5, 118.9, 118.5, 118.4, 118.3, 111.9, 110.4, 109.7, 101.8, 62.7, 52.0, 35.2, 25.7, 22.9, 18.2, 8.7, 7.9; HRMS: m/z calcd for C\(_{28}\)H\(_3\)N\(_2\) [M+H\(^+\)]: 395.2487; found: 395.2496.

Further elution of the column with EtOAc-hexane (1:39) gave the isomer 9b (14 mg, 15%) as white crystalline solid; Rf = 0.45 (EtOAc-hexane 1:19).

IR (neat): \( \nu_{max}/cm^{-1} \) 3479, 3410 (-NH), 3049, 2926, 1615, 1455, 1376, 1172, 973, 599; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 7.91 (br s, 1H), 7.60-7.00 (m, 8H), 6.22 (d, \( J = 16.3 \) Hz), 6.08 (d, \( J = 16.1 \) Hz, 1H), 5.28 (d, \( J = 9.3 \) Hz, 1H), 4.17 (q, \( J = 17.3 \) Hz, 1H), 2.80-2.75 (m, 1H), 2.35-2.25 (m, 1H), 2.20 (s, 3H), 2.17 (s, 3H), 1.8 (s, 6H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 142.6, 136.1, 133.7, 133.1, 131.4, 131.0, 129.4, 124.9, 122.9, 120.2, 119.4, 118.8, 118.5, 118.4, 117.1, 111.5, 110.3, 109.9, 101.7, 63.5, 51.9, 34.7, 25.9, 25.7, 18.2, 8.6, 7.8; HRMS: m/z calcd for C\(_{28}\)H\(_3\)N\(_2\)Na [M+Na\(^+\)]: 395.2487; found: 395.2493.

20 Example 2
Synthesis of compound 10a and 10b:

To a solution of the alcohol 8 (100 mg, 0.46 mmol) and diene 7 (156 mg, 0.46 mmol) in anhydrous CH\(_2\)Cl\(_2\) (6 ml) was added a catalytic amount of Cu(OTf)\(_2\) (32.5 mg, 0.09 mmol) and stirred magnetically for 0.5 h at RT. The progress of reaction was monitored by TLC till the starting alcohol had been completely consumed. Water (5 ml) was added to the reaction mixture, extracted with CH\(_2\)Cl\(_2\) (3 x 5 ml), washed with brine (5 ml) and dried over Na\(_2\)SO\(_4\). Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:99) as eluent furnished the isomer 10a (176 mg, 71%) as white crystalline solid;
RF = 0.5 (EtOAc-hexane 1:49); IR (neat): νmax/cm⁻¹ 2925, 1615, 1454, 1366, 1170, 967, 787, 603; ¹H NMR (CDCl₃, 200 MHz): 5 8.18 (d, J = 8.1 Hz, 1H), 7.60-6.90 (m, 12H), 6.38 (d, J = 15.8 Hz, 1H), 5.98 (d, J = 16Hz, 1H), 5.32 (d, J = 9.3 Hz, 1H), 4.38 (q, J = 17.3 Hz, 1H), 2.90-2.80 (m, 1H), 2.28-2.39 (m, 1H), 2.23 (s, 3H), 2.15 (s, 3H), 2.02 (s, 3H), 1.83 (d, J = 4.9 Hz, 6H); ¹³C NMR (CDCl₃, 50 MHz): δ 142.7, 139.3, 138.3, 136.0, 133.8, 133.6, 133.3, 133.2, 131.5, 128.8, 126.4, 124.9, 124.6, 123.5, 120.3, 119.0, 118.6, 118.5, 117.9, 114.8, 110.0, 101.8, 63.6, 51.2, 34.8, 25.7, 25.5, 18.2, 10.1, 7.8; HRMS: m/z calcd for C₃₄H₃₈N₂O₅S Na [M+Na⁺]: 557.2239; found: 557.2235.

Further elution of the column with EtOAc-hexane (1:99) gave the isomer 10b (60 mg, 24%) as white crystalline solid; RF = 0.45 (EtOAc-hexane 1:49).

IR (neat): νmax/cm⁻¹ 2923, 1614, 1452, 1372, 1171, 972, 761, 471. ¹H NMR (CDCl₃, 200 MHz): δ 8.18 (d, J = 7.3 Hz, 1H), 7.75-6.90 (m, 13H), 6.18 (d, J = 16.4 Hz, 1H), 5.32 (dt, J = 9.3, 1.4, 2.6 Hz, 1H), 4.27 (q, J = 16.9 Hz, 1H), 2.84-2.67 (m, 1H), 2.50-2.30 (m, 1H), 2.21 (s, 6H), 1.90-1.70 (m, 1H); ¹³C NMR (CDCl₃, 50 MHz): δ 142.1, 140.6, 138.2, 136.3, 133.6, 133.5, 133.4, 133.2, 131.8, 131.1, 128.9, 126.5, 125.1, 125.0, 123.7, 120.2, 120.0, 119.2, 119.0, 118.5, 115.0, 109.7, 101.8, 62.7, 52.0, 35.1, 25.7, 22.6, 18.2, 10.4, 7.81; HRMS: m/z calcd for C₅₄H₄₃N₅O₃S Na [M+Na⁺]: 557.2239; found: 557.2237.

**Example 3: Synthesis of compound 5:**

![Chemical structure](image)

To a magnetically stirred solution of the indole 5a (30 g, 110.7 mmol) in CH₂Cl₂ (130 ml) was added dichloromethyl methyl ether (34.4 ml, 387.5 mmol) followed by dropwise addition of SnCl₄ (45.4 ml, 387.5 mmol) at -78 °C, the mixture was allowed to come to -10 °C slowly over a period of lh. 1.0 N HCl (20 ml) was added to the reaction mixture and extracted with CH₂Cl₂. The organic layer is washed with brine and dried over Na₂SO₄. Evaporation of the solvent and recrystallization of the crude product from 1,2-dichloroethane furnished the aldehyde 5 (27 g, 82%) as a white crystaline solid; RF = 0.4 (EtOAc-hexane 1:9); IR (neat): νmax/cm⁻¹ 2924, 2855, 2725, 1676 (C=O), 1462, 1365, 1173, 955, 722, 601; ¹H NMR (CDCl₃, 200 MHz): 5 10.60 (s, 1H), 8.22 (dt, J = 8.3 Hz, 1H), 7.75-7.60 (m, 2H), 7.60-7.20 (m, 6H), 2.51 (s, 3H); ¹³C NMR (CDCl₃, 50 MHz): 6 185.2, 137.5, 137.0, 134.1, 133.0, 132.5, 130.6, 129.2, 129.2, 126.7, 124.8, 121.7, 115.8, 10.5; HRMS: m/z calcd for C₁₅H₁₃NO₃S [M+H⁺]: 300.0694; found: 300.0686.

**Example 4: Synthesis of compound 5'**
To a solution of the aldehyde 5 (12 g, 40.13 mmol) in anhydrous CH₂Cl₂ (200 ml) was added dry Ph₃P=CHCO₂Et (20.9 g, 60.2 mmol) and stirred magnetically for 6 h at RT. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1.5:8.5) as eluent gave the ester 5' (14 g, 95%) as white crystalline solid;

Rf = 0.45 (EtOAc-hexane 3:7); IR (neat): νmax/cm⁻¹: 2984, 1712 (0-C=O), 1623, 1445, 1371, 1170, 982, 760, 598; ¹H NMR (CDCl₃, 200 MHz): δ 8.25 (m, 2 H), 8.21 (m, 1 H), 7.75-7.60 (m, 2 H), 7.55-7.20 (m, 6 H), 6.12 (d, J = 16.2 Hz, 1 H), 4.33 (q, J = 7.14, 2 H), 2.31 (s, 3 H), 1.39 (t, J = 7.1 Hz, 3 H); ¹³C NMR (CDCl₃, 50 MHz): δ 166.40, 137.8, 137.1, 134.5, 133.8, 131.8, 131.5, 129.0, 126.7, 126.5, 124.3, 123.5, 122.6, 119.9, 115.4, 109.4, 10.9; HRMS: m/z calcd for C₁₃H₁₉NO₄SNa [M+Na⁺]: 392.0935; found: 392.0933.

Example 5: Synthesis of compound 6:

To a cold (0 °C), magnetically stirred solution of the ester 5' (10.0 g, 27.1 mmol) was added methyl magnesium iodide [prepared from magnesium turnings (2.6 g, 108.4 mmol), methyl iodide (10.1 ml, 162.6 mmol) and few crystals of iodine in anhydrous ether (50 ml)] and stirred for 2 h at RT. The reaction mixture was quenched with aq.NH₄Cl solution (50 ml) and worked up. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:4) as eluent furnished the tertiary alcohol 6 (7.8 g, 81%) as a white solid;

Rf = 0.4 (EtOAc-hexane 2:3); IR (neat): νmax/cm⁻¹: 2953, 1583, 1455, 1170, 963, 725, 595; ¹H NMR (CDCl₃, 200 MHz): δ 8.20 (dt, J = 7.20, 1 H), 7.75-7.60 (m, 2 H), 7.50-7.15 (m, 6 H), 7.00-6.85 (m, 1 H), 5.94 (d, J = 16.2 Hz, 1 H), 2.18 (br s, 1 H), 2.18 (s, 3 H), 1.50 (s, 6 H); ¹³C NMR (CDCl₃, 50 MHz): δ 144.4, 138.4, 136.3, 133.9, 131.5, 131.9, 128.9, 126.7, 125.0, 123.7, 119.1, 118.2, 117.1, 115.1, 71.2, 29.7, 10.2; HRMS: m/z calcd for C₂₀H₂₁N₃O₅SNa [M+Na⁺]: 378.1142; found: 378.1139.

Example 6: Synthesis of compound 7:
To a solution of the alcohol 6 (3.6 g, 10.14 mmol) in anhydrous THF (50 ml) and Et₃N (8.45 ml, 60.84 mmol) under N₂ atmosphere was added MsCl (2.35 ml, 30.42 mmol) slowly over a period of 5 min at 0 °C. The solution was allowed to warm to RT for about 1.5 h and then refluxed for 30 min. The precipitate formed is filtered off using ethyl acetate affording a brown viscous liquid. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:9) as eluent furnished the diene 7 (2.8 g, 82%) as a white solid;

\[ Rf = 0.5 \text{ (EtOAc-hexane 1:9); IR (neat): } \nu_{\text{max}}/\text{cm}^{-1} = 3414, 1644, 1449, 1215, 1022, 756.5, 666.9; ^1H NMR (CDCl₃, 500 MHz): } δ = 9.24 (br s, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.30 (d, J = 7.9 Hz, 1H), 7.13 (ddd, J = 1.2 Hz, 7.3 Hz, 8.2 Hz, 1H), 7.01 (ddd, J = 0.9 Hz, 7.0 Hz, 7.9 Hz, 1H), 6.78 (d, J = 16.2 Hz, 1H), 6.71 (d, J = 16.2 Hz, 1H), 5.11 (d, J = 19.8 Hz, 2H), 2.33 (s, 3H), 2.01 (s, 3H); ^13C NMR (CDCl₃, 120 MHz): } δ = 143.5, 137.8, 133.6, 130.3, 130.2, 123.8, 121.6, 119.4, 119.1, 118.1, 115.2, 18.5, 10.6; HRMS: m/z calcd for C₂₀H₂₂N₂O₂ [M+H⁺]: 338.1214; found: 338.1208.

Example 7: Synthesis of compound 4:

To a solution of the protected diene 7 (2.5 g, 7.4 mmol) in MeOH (30 ml) is added NaOH (3 g, 74.2 mmol) in H₂O (10 ml) and the reaction mixture was heated to 70 °C for 3 h. Excess MeOH was removed under reduced pressure. The residue was washed with ether (3 x 20 ml). The organic extracts were combined, washed with brine (20 ml) and dried over anhydrous Na₂SO₄. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:3) as eluent gave the diene 4 (1.1 g, 75%) as a yellow solid;

\[ Rf = 0.35 \text{ (EtOAc-hexane 1:1); IR (neat): } \nu_{\text{max}}/\text{cm}^{-1} = 3414, 1644, 1449, 1215, 1022, 756.5, 666.9; ^1H NMR (CDCl₃, 500 MHz): } δ = 143.5, 137.8, 133.6, 130.3, 130.2, 123.8, 121.6, 119.4, 119.1, 118.1, 115.2, 18.5, 10.6; HRMS: m/z calcd for C₂₀H₂₂N₂O₂ [M+H⁺]: 338.1214; found: 338.1208.
123.7, 120.0, 119.5, 117.2, 112.4, 111.4, 18.6, 8.7; HRMS: m/z calcd for C_{4}H_{5}N [M+ H\textsuperscript{+}]: 198.1204; found: 198.0914.

Example 8: Synthesis of compound 8:

To a solution of the alcohol 6 (6 g, 16.9 mmol) in anhydrous methanol (50 ml) was added Na\textsubscript{2}HPO\textsubscript{4} (9.6 g, 67.6 mmol) and Na-Hg (15.5 g, 67.6 mmol). The reaction mixture was stirred for 1 h at RT until all of the amalgam had become converted to liquid mercury.

Water (20 ml) and ether (40 ml) were added and the supernatant was decanted. The residue was washed with ether (3 x 20 ml). The organic extracts were combined, washed with brine (20 ml) and dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:3) as eluent gave the alcohol 8 (3.3 g, 91%) as a yellow solid:

\[ Rf = 0.35 \text{ (EtOAc-hexane 1:1); IR (neat):} \nu_{\text{max/cm}^{-1}} = 3362 \text{ (OH), 3056 (NH), 2864, 1583, 1377, 1086, 786;} \text{ \textsuperscript{1}H NMR (CDCl}_3, 200 MHz):} \delta = 7.98 \text{ (br s, 1H), 7.60-7.00 (m, 4H), 6.74 (d,} J = 16.3 \text{ Hz, 1H), 6.08 (d,} J = 16.2 \text{ Hz, 1H), 2.33 (s, 3 H), 1.64 \text{ (br s, 1H), 1.46 (s, 6 H);} \text{ \textsuperscript{13}C NMR (CDCl}_3, 50 MHz):} \delta = 136.27, 134.78, 131.38, 129.61, 122.83, 119.37, 118.88, 115.73, 111.49, 110.38, 71.23, 30.04, 8.65; \text{ HRMS: m/z calcd for C}_{4}\text{H}_5\text{N [M-OH]: 198.1283; found: 198.1281.} \]

Example 9: Synthesis of compound 9a:

To a solution of the 10a (50 mg, 0.09 mmol) in anhydrous methanol (6 ml) was added Na\textsubscript{2}HPO\textsubscript{4} (56 mg, 0.36 mmol) and Na-Hg (82 mg, 0.36 mmol). The reaction mixture was stirred for 1 h at RT until all of the amalgam had become liquid mercury. Water (5 ml) and ether (10 ml) were added and the supernatant solution was decanted, extracted with
ether (3 x 5 ml), washed with brine (5 ml) and dried over Na$_2$SO$_4$. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:39) furnished the compound 9a (35 mg, 94%) as a white solid; $R_f = 0.5$ (EtOAc-hexane 1:19); whose data (IR, $^1$H NMR, $^{13}$C NMR and HRMS) was identical with earlier compound 9a obtained from dimerization of terr-alcohol 8.

Example 10: Synthesis of compound 9b:

To a solution of the 10b (50 mg, 0.09 mmol) in anhydrous methanol (6 ml) was added Na$_2$HPO$_4$ (56 mg, 0.36 mmol) and Na-Hg (82 mg, 0.36 mmol). The reaction mixture was stirred for 1 h at RT until all of the amalgam had become converted into liquid mercury. Water (5 ml) was added to the reaction mixture, extracted with ether (3 x 5 ml), washed with brine (5 ml) and dried over Na$_2$SO$_4$. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:39) as eluent gave the compound 9b (35 mg, 94%) as a white solid $R_f = 0.45$ (EtOAc-hexane 1:19); whose data (IR, $^1$H NMR, $^{13}$C NMR and HRMS) was identical with earlier compound 9b obtained from dimerization of tert-alcohol 8.

Example 11: Synthesis of compound 8' :

To a cold (0 °C), magnetically stirred solution of the ester 5' (1 g, 2.71 mmol) was added methyl magnesium iodide [prepared from magnesium turnings (395 mg, 16.3 mmol), ethyl bromide (1.4 ml, 19.0 mmol) and few crystals of iodine in anhydrous ether (15 ml)]
and stirred for 2 h at RT. The reaction mixture was then quenched with aq. NH₄Cl solution (10 ml) and worked up. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:4) as eluent furnished the tertiary alcohol 8' (800 mg, 80%) as a white solid; Rf = 0.4 (EtOAc - hexane 1:4). IR (neat): νmax/cm⁻¹ 1879, 1724, 1584, 1449, 1372, 1271, 1174, 1091, 1023, 980.4, 758.9, 592.0; ¹H NMR (CDCl₃, 200 MHz): δ 8.19 (dd, J = 1.5, 7.1 Hz, 1H), 7.74-7.68 (m, 2H), 7.49-7.19 (m, 6H), 6.99 (d, J = 16.9 Hz, 1H), 5.85 (d, J = 16.3 Hz, 1H), 2.21 (s, 3H), 1.72 (q, J = 7.6, 15.3 Hz, 4H), 0.99 (t, J = 7.5 Hz, 6H); ¹³C NMR (CDCl₃, 50 MHz): δ 142.1, 138.4, 136.1, 134.3, 133.4, 131.8, 128.8, 126.5, 124.8, 123.6, 119.0, 118.8, 117.9, 115.0, 75.9, 33.0, 10.3, 7.9; HRMS-ESI: m/z calcd for C₂₂H₂₅NO₃S Na [M+Na⁺]: 422.1555; found: 422.1107.

Example 12: Synthesis of compound 8''

To a solution of the alcohol 8' (230 mg, 0.59 mmol) in anhydrous methanol (5 ml) was added Na₂HPO₄ (339 mg, 2.38 mmol) and Na-Hg (548 mg, 2.36 mmol). The reaction mixture was stirred for 1 h at RT until all of the amalgam had become converted to liquid mercury. Water (5 ml) and ether (10 ml) were added and the supernatant was decanted. The residue was washed with ether (3 x 5 ml). The organic extracts were combined, washed with brine (5 ml) and dried over anhydrous Na₂SO₄. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:4) as eluent gave the alcohol 8'' (148 mg, 91%) as a yellow solid; Rf = 0.5 (EtOAc-hexane 1:4); IR (neat): νmax/cm⁻¹ 2929, 1654, 1523, 1457, 1246, 872.6, 788.2; ¹H NMR (CDCl₃, 200 MHz): 6 9.18 (br s, 1H), 7.46 (d, J = 7.7 Hz, 1H), 7.28 (d, J = 7.7 Hz, 1H), 7.14-6.96 (m, 2H), 6.69 (d, J = 16.2 Hz, 1H), 6.07 (d, J = 16.3 Hz, 1H), 2.3 (s, 3H), 1.61 (q, J = 7.2, 15.2 Hz, 4H), 0.89 (t, J = 7.6 Hz, 6H); ¹³C NMR (CDCl₃, 50 MHz): δ 137.8, 135.5, 133.8, 130.7, 123.5, 120.1, 119.7, 117.9, 111.7, 110.6, 76.54, 34.6, 9.0, 8.7; HRMS-ESI: m/z calcd for C₄H₆INO [M+H⁺]: 244.1701; found: 244.1709.

Example 13: Synthesis of compound 10d

10c

MeMgl, Et₂O

0 °C - RT, 2 h, 88%

10d
To a magnetically stirred solution of methylmagnesium iodide, [prepared from
magnesium turnings (2.8 g, 112.8 mmol), methyl iodide (9.37 ml, 150.4 mmol) and few
crystals of iodine in anhydrous ether (50 ml)] was added slowly a mixture of the ester
10c (11 g, 37.6 mmol) in anhydrous ether (40 ml). The reaction mixture was stirred for 2
h at RT. It was then quenched with aq. NH₄Cl solution (40 ml), extracted with ethyl
acetate (3 x 15 ml), washed with brine and dried over Na₂SO₄. Evaporation of the solvent
and purification of the residue on a silica gel column using EtOAc-hexane (2:8) as eluent
furnished the alcohol 10d (9.2 g, 88%) as a white solid.

Example 14: Synthesis of compound 10e:

To a solution of the

10d (8.0 g, 31.7

anhydrous THF

(60 ml) and Et₃N (26.3 ml, 190.6 mmol) under \( \text{N}_2 \) atmosphere was added MsCl (7.35 ml,
95.1 mmol) slowly over a period of 5 min at 0 °C. The solution was allowed to warm at RT
for 1.5 h and then refluxed for 30 min. The precipitate formed was filtered off using ethyl
acetate affording a colourless viscous liquid. Evaporation of the solvent and purification
of the residue on silica gel column using EtOAc-hexane (1:9) as eluent furnished the diene
10e (6.3 g, 85%) as a colourless viscous liquid.

Example 15: Synthesis of compound 10g:
To a magnetically stirred solution of methyl magnesium iodide, [prepared from magnesium turnings (3.4 g, 138.1 mmol), methyl iodide (11.5 ml, 184.4 mmol) and few crystals of iodine in anhydrous ether (50 ml)] was added slowly a mixture of the ester 1Of (13 g, 46.1 mmol) in anhydrous ether (50 ml). The reaction mixture was stirred for 2 h at RT. It was then quenched withaq. NH₄Cl solution (50 ml), extracted with ethyl acetate (3 x 15 ml), washed with brine and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc-hexane (1:4) as eluent furnished the alcohol 1Og (10.5 g, 90%) as a viscous liquid.

\[ Rf = 0.3 \text{ (EtOAc-hexane 1:3); IR ( neat): } v_{\text{max/cm}^{-1}} \text{ 3402 (OH), 2927, 2856, 1607, 1509, 1216, 1174, 1024, 756, 676, 668; } ^1H \text{ NMR (200 MHz, CDCl}_3\text{): } \delta 7.50-7.25 \text{ (m, 7H), 7.92 (d, } J = 8.8 \text{ Hz, 2H), 6.15 (d, } J = 16.1 \text{ Hz, 1H).} \]

\[ 1C \text{ NMR (50 MHz, CDCl}_3\text{): } \delta 158.2, 136.9, 135.5, 129.8, 128.6, 127.9, 127.6, 127.5, 127.4, 125.7, 114.9, 71.03, 69.95, 29.87, 18.60; \text{ HRMS-ESI: m/z calcd for } C_{18}H_{20}O_2K [M+K^+] = 307.1463; \text{ found: 307.0933.} \]

**Example 16: Synthesis of compound 1Oh:**

To a solution of the alcohol 1Og (4.0 g, 14.9 mmol) in anhydrous THF (40 ml) and Et₃N (2.4 ml, 89.6 mmol) under N₂ atm was added MsCl (3.5 ml, 44.7 mmol) slowly over a period of 5 min at -78 °C. The solution was allowed to warm to RT for 1.5 h and then refluxed for 30 min. The precipitate formed was filtered off using ethyl acetate affording a viscous liquid. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:19) as eluent furnished the diene 1Oh (3.1 g, 83%) as a viscous liquid.

\[ Rf = 0.3 \text{ (EtOAc-hexane 1:19); IR ( neat): } v_{\text{max/cm}^{-1}} \text{ 2975, 2400, 1601, 1509, 1239, 1216, 1025, 963, 668, 541; } ^1H \text{ NMR (200 MHz, CDCl}_3\text{): } \delta 7.50-7.15 \text{ (m, 7H), 7.92 (t of } d J = 8.8 \text{ and 2.9 Hz, 2H), 6.76 (d, } J = 16.1Hz, 1H), 6.46 (d, } J = 16.1 \text{ Hz, 1H), 6.46 (d, } J = 16.1 \text{ Hz,} \]

27
2-Formyl-3-methyl-1-phenylsulphonyl indole 5 (5.0 g, 16.7 mmol) was added to powdered potassium hydroxide (4.7 g, 83.6 mmol) in ethanol (150 ml) and the mixture was stirred under reflux for 45 min and then concentrated under reduced pressure. Water (50 ml) was added and the reaction mixture was extracted with CH$_2$Cl$_2$ (3 x 50 ml), dried over Na$_2$SO$_4$. Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc-hexane (1:19) as eluent furnished the aldehyde 10i (3.1 g, 90%) as a yellow solid.

$$R_f = 0.35 \text{ (EtOAc-hexane 1:9)}.$$ IR (neat): $\nu$ = 2926, 2850, 2735, 1680 (C=O), 1462, 1365, 1174, 960, 724, 601; $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 10.18 (s, 1H), 9.22 (s, 1H), 7.80 (d, $J = 8.2$ Hz, 1H), 7.47-7.33 (m, 2H), 7.24-7.12 (m, 1H), 5.02 (s, 2H), 3.66 (q, $J = 7.0$ Hz, 2H), 1.28 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ = 181.9, 137.2, 132.9, 127.5.

**Example 18:** Synthesis of compound 10j:

To a magnetically stirred solution of the indole 10i (1.4 g, 6.86 mmol) in THF (15 ml) was added KOH powder (1.9 g, 34.3 mmol) followed by dropwise addition of PhSO$_2$Cl (2.6 ml, 20.6 mmol) at 0 °C, and stirred magnetically for 6 h at RT. Water (20 ml) was then added to the reaction mixture, extracted with EtOAc (3 x 20 ml), washed with brine (20 ml) and dried over Na$_2$SO$_4$. Evaporation of the solvent and...
purification of the residue on silica gel column using EtOAc-hexane (1:9) as eluent furnished the compound \textbf{10j} (2.1 g, 91%) as white crystalline solid;

\[ R' = 0.3 \text{ (EtOAc-hexane 1:9); IR (neat): } \nu \text{ cm}^{-1} \text{ 2974, 2926, 1677, 1543, 1372, 1175, 1088, 751, 724, 685; } ^1H \text{ NMR (200 MHz, CDCl}_3\text{): } 6 \text{ 10.61 (s, 1H), 8.21 (t of } d, J = 8.5 \text{ and 0.8 Hz, 1H), 7.97 (t of } d, J = 8.0 \text{ and 1.0 Hz, } 1H \text{, 7.75-7.67 (m, 2H), 7.58-7.47 (m, 2H), 7.45-7.25 (m, 3H), 4.94 (s, 2H), 1.50 (q, } J = 7.0 \text{ Hz, 2H), 1.20 (t, } J = 7.0 \text{ Hz, 3H); } ^{13}C \text{ NMR (50 MHz, CDCl}_3\text{): } \delta \text{ 153.3, 137.5, 137.1, 132.7, 126.3, 103.3, 70.9, 60.9, 56.0, 29.9; HRMS-ESI: m/z calcd for C\text{14}H\text{10}N\text{O}_2\text{S}[\text{M+H}^+: 344.0957; found : 344.0955.} \]

\textbf{Example 19: Synthesis of compound 10k:}

![Chemical structure of 10j](image1)

To a solution of the aldehyde \textbf{10j} (11 g, 32.1 mmol) in anhydrous CH\text{2}Cl\text{2} (200 ml) was added dry Ph\text{3}P=CHCO\text{2}Et (16.8 g, 48.2 mmol) and stirred magnetically for 6 h at RT. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (2:8) as eluent gave the ester \textbf{10k} (12.5 g, 94%) as white crystalline solid.

\[ R' = 0.35 \text{ (EtOAc-hexane 3:7); IR (neat): } \nu \text{ cm}^{-1} \text{ 3019, 1708 (OC=O), 1630, 1448, 1374, 1215, 758, 669; } ^1H \text{ NMR (200 MHz, CDCl}_3\text{): } 6 \text{ 8.30-8.15 (m, 2H), 7.80-7.60 (m, 3H), 7.55-7.20 (m, 5H), 6.30 (d, } J = 15.9 \text{ Hz, 1H), 4.55 (s, 2H), 4.33 (q, } J = 7.1 \text{ Hz, 2H), 3.51 (q, } J = 7.1 \text{ Hz, 2H), 1.39 (t, } J = 7.1 \text{ Hz, 3H), 1.20 (t, } J = 7.1 \text{ Hz, 3H); } ^{13}C \text{ NMR (50 MHz, CDCl}_3\text{): } \delta \text{ 175.4, 175.1, 162.6, 147.8, 130.2, 129.7, 116.5, 95.7, 81.8, 81.1, 69.9, 69.4, 67.3, 67.2, 67.1, 66.7, 66.6, 60.3, 52.8, 52.7, 40.7, 40.1, 28.5, 27.7, 26.8, 24.5, 23.4; HRMS-ESI: calcd for C\text{2}12H\text{14}N\text{O}_2\text{SNa}[\text{M+Na}^+: 436.195; found : 436.1194.} \]

\textbf{Example 20: Synthesis of compound 10l:}

![Chemical structure of 10k](image2)

To a cold (0 °C), magnetically stirred solution of the ester \textbf{10k} (10.0 g, 24.2 mmol) was added methyl magnesium iodide [prepared from magnesium turnings (2.6 g, 72.6 mmol), methyl iodide (10.1 ml, 96.8 mmol) and few crystals of iodine in anhydrous ether (75 ml)]
and stirred for 2 h at RT. The reaction mixture was then quenched with aq. NH₄Cl solution (50 ml) and worked up. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (2:8) as eluent furnished the tertiary alcohol 101 (8.0 g, 83%) as a waxy solid:

\[ Rf = 0.3 \text{ (EtOAc-hexane 2:3); IR (neat): } v_{\text{max}}/\text{cm}^{-1} 2853, 1583, 1455, 1170, 963, 725, 595; \]

\[ ^1H \text{ NMR (200 MHz, CDCl}_3): \delta 8.20 \text{ (dd, } J = 7.3, 1.5 \text{ Hz, 1H}), 7.74 \text{ (d, } J = 7.3 \text{ Hz, 2H}), 7.65-7.15 \text{ (m, 6H)}, 7.02 \text{ (d, } J = 16.0 \text{ Hz, 1H}), 4.48 \text{ (s, 2H)}, 3.48 \text{ (q, } J = 7.0 \text{ Hz, 2H}), 1.48 \text{ (s, 6H)}, 1.18 \text{ (t, } J = 7.0 \text{ Hz, 3H); } ^{13}C \text{ NMR (CDCl}_3, 50 \text{ MHz):} 164.2, 138.4, 137.3, 136.1, 133.8, 130.4, 129.0, 126.7, 125.0, 123.9, 119.7, 1189.4, 116.0, 114.6, 71.1, 65.6, 29.7, 15.2; \]


**Example 21: Synthesis of compound 10m:**

![Diagram](image)

To a solution of alcohol 101 (6.0 g, 15.0 mmol) in anhydrous THF (40 ml) and Et₃N (12.5 ml, 90.0 mmol) under N₂ atmosphere was added MsCl (3.5 ml, 45.0 mmol) slowly over a period of 4 min at 0°C. The solution was allowed to warm at RT for 1.5 h and then refluxed for 30 min. The precipitate formed was filtered off using ethyl acetate affording a brown viscous liquid. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:19) as eluent furnished the diene 10m (5.0 g, 87%) as a white solid:

\[ Rf = 0.40 \text{ (EtOAc-hexane 1:9); IR (neat): } v_{\text{max}}/\text{cm}^{-1} 3019, 1646, 1449, 1363, 1216, 1088, 586; \]

\[ ^1H \text{ NMR (200 MHz, CDCl}_3): \delta 8.21 \text{ (d, } J = 8.2 \text{ Hz, 1H}), 7.80-7.53 \text{ (m, 3H)}, 7.50-7.16 \text{ (m, 5H)}, 7.05 \text{ (d, } J = 16.1 \text{ Hz, 1H}), 6.61 \text{ (d, } J = 16.1 \text{ Hz, 1H}), 5.17 \text{ (d, } J = 5.6 \text{ Hz, 2H}), 4.51 \text{ (s, 2H)}, 3.50 \text{ (q, } J = 7.0 \text{ Hz, 2H}), 2.07 \text{ (s, 3H)}, 1.13 \text{ (t, } J = 7.1 \text{ Hz, 3H); } ^{13}C \text{ NMR (CDCl}_3, 50 \text{ MHz):} 142.1, 139.0, 138.3, 138.1, 136.3, 133.8, 130.7, 129.0, 126.8, 125.1, 124.0, 119.7, 119.1, 118.7, 118.2, 114.8, 65.7, 63.5, 18.5, 15.3; \]


**Example 22: Synthesis of compound 11:**

![Diagram](image)

\[ \text{C}_{11} \text{H}_{13} \text{N}_{5} \text{O}_{4} \text{S}_{2} \text{Na} \]
To a solution of the alcohol 8 (40 mg, 0.16 mmol) and diene 7 (55 mg, 0.16 mmol) in anhydrous CH$_2$Cl$_2$ (5 ml) was added a catalytic amount of Cu(OTf)$_2$ (11 mg, 0.03 mmol) and stirred magnetically for 0.5 h at RT. The progress of reaction was monitored by TLC till the starting alcohol had been completely consumed. Water (10 ml) was then added to the reaction mixture, extracted with CH$_2$Cl$_2$ (3 x 5 ml), washed with brine (5 ml) and dried over Na$_2$SO$_4$. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:49) as eluent furnished the isomer 11 (76 mg, 82%) as white crystalline solid.

*RT* = 0.4 (EtOAc-hexane 1:49); IR (neat) : $\nu_{max}$/cm$^{-1}$ 2970, 1641, 1454, 1371, 1215, 1022, 668; $^1$H NMR (500 MHz, CDCl$_3$): 6.821 (d, J = 8.4 Hz, 1H), 7.59 (t, J = 4.4 Hz, 1H), 7.46 (t, J = 4.1 Hz, 1H), 7.39-7.18 (m, 5H), 7.11-7.06 (m, 2H), 7.02 (t, J = 7.9 Hz, 2H), 6.35 (d, J = 16.1 Hz, 1H), 5.99 (d, J = 16.1 Hz, 1H), 5.26 (d, J = 9.5 Hz, 1H), 4.40 (q, J = 8.8 Hz, 1H), 2.83 (dd, J = 12.6 and 7.7 Hz, 1H), 2.40-2.26 (m, 2H), 2.24 (s, 3H), 2.21-2.09 (m, 6H), 2.02 (s, 3H), 1.07 (t, J = 7.5 Hz, 3H), 1.06 (t, J = 7.5 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): 6

144.9, 142.9, 139.4, 138.3, 136.1, 133.8, 133.3, 131.6, 131.4, 128.9, 126.5, 124.9, 123.6, 122.7, 120.3, 119.0, 118.6, 118.5, 117.9, 114.9, 109.9, 101.9, 63.7, 51.7, 34.4, 29.2, 25.5, 23.7, 13.7, 12.9, 10.2, 7.9; HRMS-ESI: m/z calcd for $\text{C}_{19}\text{H}_{17}\text{NOS}$ [M+H$^+$]: 563.2732; found: 563.2736.

**Example 23: Synthesis of compound 12:**

![Synthesis Diagram]
To a solution of the alcohol 8 (40 mg, 0.186 mmol) and diene 10m (68 mg, 0.204 mmol) in anhydrous CH₂Cl₂ (5 ml) was added a catalytic amount of Cu(OTf)₂ (11 mg, 0.03 mmol) and stirred magnetically for 0.5 h at RT. The progress of reaction was monitored by TLC till the starting alcohol had been completely consumed. Water (5 ml) was then added to the reaction mixture, extracted with CH₂Cl₂ (3 x 5 ml), washed with brine (5 ml) and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:19) eluent furnished the isomer 12 (86 mg, 81 %) as white crystalline solid.

\[ R̅ = 0.4 \text{ (EtOAc-hexane 1:19); IR (neat); ν^\text{cm}^{-1} 2977, 1450, 1377, 1174, 1089, 929, 669; } \]

\[ ^1\text{H NMR (200 MHz, CDCl}_3\text{: }\delta 8.17 (d, J = 7.5, 1.3 Hz, 1H), 7.60-7.48 (m, 2H), 7.45-7.16 (m, 6H), 7.14-7.00 (m, 4H), 6.37 (d, J = 15.8 Hz 1H), 6.17 (d, J = 15.9 Hz, 1H), 5.30 (septet of a doublet, J = 9.5 and 1.3 Hz, 1H), 4.38 (d, J = 2.1 Hz, 2H), 4.45-4.25 (m, 1 H), 3.45-3.20 (m, 2 H), 2.80 (dd, J = 12.5 and 7.5 Hz, 1H), 3.45-3.20 (m, 2 H), 2.30 (dd, J = 12.5 and 7.5 Hz, 1H), 2.33 (dd, J = 12.6 and 9.6 Hz.), 2.03 (s, 3H), 1.82 (s, 6H), 1.12 (t, J = 7.0 Hz, 3H); } \]

\[ ^{13}\text{C NMR (50 MHz, CDCl}_3\text{: }\delta 142.0, 140.7, 138.4, 136.7, 135.9, 129.7, 116.5, 133.9, 133.7, 133.6, 131.55, 130.2, 129.0, 126.5, 125.0, 124.6, 123.7, 120.3, 119.5, 118.6, 118.2, 117.5, 114.5, 110.0, 102.0, 65.6, 63.6, 63.3, 51.2, 34.8, 25.7, 25.4, 18.2, 15.2, 7.8; \]

\[ \text{HRMS-ESI: calcd for C}_{36}H_{38}N_{2}O_{3}S [M+H^+] 579.2681; found: 579.2695.} \]

**Example 24: Synthesis of compound 13:**

![Chemical structure of compounds 8, 10m, 12, and 13](image)

To a solution of the alcohol 8" (50 mg, 0.205 mmol) and diene 10m (69 mg, 0.205 mmol) in anhydrous CH₂Cl₂ (5 ml) was added a catalytic amount of Cu(OTf)₂ (15 mg, 0.04 mmol) and stirred magnetically for 0.5 h at RT. The progress of reaction was monitored by TLC till the starting alcohol had been completely consumed. Water (5 ml) was then added to the reaction mixture, extracted with CH₂Cl₂ (3 x 5 ml), washed with brine (5 ml) and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on silica gel
column using EtOAc-hexane (1:19) as eluent furnished the isomer 13 (106 mg, 85%) as white crystal line solid.

\[ Rf = 0.4 \text{ (EtOAc-hexane 1:19); } \]

**IR (neat):** ν<sub>max</sub>/cm<sup>-1</sup> 2975, 1449, 1046, 929, 669; **1H NMR** (200 MHz, CDCl<sub>3</sub>): 6 8.17 (dd, <i>j</i> = 7.5, 1.3 Hz, 1H), 7.60-7.49 (m, 2H), 7.45-7.16 (m, 6H), 7.14-7.00 (m, 4H), 6.37 (d, <i>j</i> = 15.8 Hz, 1H), 6.18 (d, <i>j</i> = 15.7 Hz, 1H), 5.26 (d, <i>j</i> = 9.6 Hz, 1H), 4.38 (d, <i>j</i> = 2.9, 2H), 4.45-4.25 (m, 1H), 3.60-3.17 (m, 2H), 2.79 (dd, <i>j</i> = 12.5 and 7.5 Hz, 1H), 2.45-2.09 (m, 9H), 2.04 (s, 3H), 1.12 (t, <i>j</i> = 7.0 Hz), 2.80 (dd, <i>j</i> = 12.5, 7.5 Hz, 1H), 2.33 (dd, <i>j</i> = 12.6, 9.6 Hz), 2.03 (s, 3H), 1.82 (s, 6H), 1.12 (t, <i>j</i> = 7.0 Hz, 3H); **13C NMR** (50 MHz, CDCl<sub>3</sub>): δ 144.9, 142.7, 140.7, 138.4, 136.8, 135.9, 133.8, 133.5, 131.5, 130.2, 129.0, 126.5, 125.0, 123.7, 122.6, 120.4, 119.5, 118.6, 118.2, 117.6, 114.5, 110.0, 102.12, 65.6, 63.3, 51.7, 34.4, 29.125.3, 23.7, 15.2, 13.7, 12.9, 7.9; **HRMS** (ESI) m/z calc'd for C<sub>28</sub>H<sub>42</sub>N<sub>2</sub>O<sub>3</sub>S [M+H<sup>+</sup>]: 607.2994; found: 607.2994.

**Example 25: Synthesis of compound 14**

To a solution of the alcohol 8 (40 mg, 0.19 mmol) and diene 10e (43 mg, 0.19 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (5 ml) was added a catalytic amount of Cu(OTf)<sub>2</sub> (11 mg, 0.03 mmol) and stirred magnetically for 0.5 h at RT. The progress of reaction was monitored by TLC till the starting alcohol had been completely consumed. Water (5 ml) was then added to the reaction mixture, extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 5 ml), washed with brine (5 ml) and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:4) as eluent furnished the mixture of isomer 14 (64 mg, 75%) as colourless oil.

\[ Rf = 0.4 \text{ (EtOAc-hexane 1:4); } \]

**IR (neat):** ν<sub>max</sub>/cm<sup>-1</sup> 2924, 1585, 1420, 1129, 1044, 929, 669; **1H NMR** (200 MHz, CDCl<sub>3</sub>): δ 7.60-7.42 (m, 1H), 7.35-7.20 (m, 1H), 7.17-6.92 (m, 2H), 6.63 (s, 0.72H), 6.54 (s, 0.28H), 6.50 (s, 1.16H), 6.45 (d, <i>j</i> = 16.1 Hz, 0.46H), 6.31 (d, <i>j</i> = 16.1 Hz, 0.63H), 5.90 (d, <i>j</i> = 16.1Hz, 0.63H), 5.27 (d, <i>j</i> = 9.4Hz, 1H), 4.00-3.45 (m, 1H), 3.85 (s, 3H), 3.82 (d, <i>j</i> = 3.2 Hz, 6H), 2.85-2.50 (m, 1H), 2.45-2.23 (m, 1H), 2.20 (dd, <i>j</i> = 1.0 Hz, 3H), 1.90 (s, 2H), 1.80 (s, 6H), 1.58 (s, 1H); **13C NMR** (50 MHz, CDCl<sub>3</sub>): 5 153.4,
Example 26: Synthesis of compound 15

To a solution of the alcohol 8" (57 mg, 0.23 mmol) and diene 10e (55 mg, 0.23 mmol) in anhydrous CH₂Cl₂ (5 ml) was added a catalytic amount of Cu(OTf)₂ (15 mg, 0.04 mmol) and stirred magnetically for 0.5 h at RT. The progress of reaction was monitored by TLC till the starting alcohol had been completely consumed. Water (5 ml) was then added to the reaction mixture, extracted with CH₂Cl₂ (3 x 5 ml), washed with brine (5 ml) and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:9) as eluent furnished the mixture of isomers 15 (81 mg, 75 %) as colourless oil

Rf = 0.35 (EtOAc-hexane 1:9); IR (neat): νmax/cm⁻¹ 2965, 2934, 2875, 1582, 1454, 1340, 1242, 1127, 1009, 813, 665; ¹H NMR (200 MHz, CDCl₃): δ 7.60-7.42 (m, 1H), 7.35-7.20 (m, 1H), 7.17-6.92 (m, 2H), 6.63 (s, 0.22H), 6.54 (s, 0.28H), 6.50 (s, 0.28H), 6.45 (d, J = 16.1 Hz, 0.40H), 6.33 (d, J = 16.1 Hz, 0.63H), 5.99 (d, J = 16.1 Hz, 0.63H), 5.23 (d, J = 9.7 Hz, 1H), 4.35-4.00 (m, 1H), 3.85 (s, 3H), 3.82 (d, J = 3.5 Hz, 6H), 2.75 (d, J = 12.5, 7.8 Hz, 0.6H), 2.60 (d, J = 12.5, 7.8 Hz, 0.40H), 2.50-2.00 (m, 8H), 1.90 (s, 1.8H), 1.65 (dd, J = 18.8 Hz, 1.8H), 1.15-0.98 (m, 6H); ¹³C NMR (50 MHz, CDCl₃): δ 153.4, 153.3, 144.4, 144.2, 142.8, 142.1, 137.8, 137.7, 134.2, 133.6, 133.5, 132.8, 132.3, 132.2, 131.4, 131.1, 129.1, 127.5, 123.0, 122.9, 120.2, 118.4, 118.3, 110.1, 109.9, 103.5, 103.4, 101.8, 101.6, 63.5, 62.6, 60.9, 56.1, 56.1, 52.6, 52.3, 34.8, 34.2, 29.1, 26.3, 23.6, 22.9, 13.6, 12.9, 7.9; HRMS-ESI: calcd for C₃₈H₇N0₃ [M+H⁺] 460.2852; found: 460.2842.
Example 27: Synthesis of compound 16

To a solution of alcohol 8 (50 g, 0.23 mmol) and diene 10h (58 mg, 0.23 mmol) in anhydrous CH₂Cl₂ (5 ml) was added a catalytic amount of Cu(OTf)₂ (15 mg, 0.04 mmol) and stirred magnetically for 0.5 h at RT. The progress of reaction was monitored by TLC till the starting alcohol had been completely consumed. Water (5 ml) was then added to the reaction mixture, extracted with CH₂Cl₂ (3 x 5 ml), washed with brine (5 ml) and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:49) as eluent furnished the mixture of isomers 16 (60 mg, 74 %) as white crystalline solid;

<chemical structure image>

m/z calcd for C₃₁H₃₃NONa [M+Na⁺]: 470.2460; found: 470.2463.

Example 28: Synthesis of compound 17

To a solution of the alcohol BnO-8'' (40 mg, 0.23 mmol) and diene 10h (58 mg, 0.23 mmol) in anhydrous CH₂Cl₂ (5 ml) was added a catalytic amount of Cu(OTf)₂ (15 mg, 0.04 mmol) and stirred magnetically for 0.5 h at RT. The progress of reaction was monitored by TLC till the starting alcohol had been completely consumed. Water (5 ml) was then added to the reaction mixture, extracted with CH₂Cl₂ (3 x 5 ml), washed with brine (5 ml) and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:49) as eluent furnished the mixture of isomers 17 (60 mg, 74 %) as white crystalline solid;

<chemical structure image>
0.164 mmol) and diene lOh (41 mg, 0.164 mmol) in anhydrous CH₂Cl₂ (5 ml) was added a catalytic amount of Cu(OTf)₂ (11 mg, 0.03 mmol) and stirred magnetically for 0.5 h at Rt. The progress of reaction was monitored by TLC till the starting alcohol had been completely consumed. Water (5 ml) was then added to the reaction mixture, extracted with CH₂Cl₂ (3 x 5 ml), washed with brine (5 ml) and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:4) as eluent furnished the mixture of isomer 17 (66 mg, 86 %) as white crystalline solid.

**Example 29: Synthesis of compound 21**

![Reaction Scheme](image)

To a magnetically stirred solution of the N-protected tryptophol 20 (25 g, 83.05 mmol) in CH₂Cl₂ (200 ml) was added pyridine (36.45 ml, 415.3 mmol), Ac₂O (39.2 ml, 415.3 mmol) and DMAP (2 g, 16.6 mmol). The reaction mixture was stirred for 6 h at RT and extracted with CH₂Cl₂, washed with brine, dil. HCl and dried over Na₂SO₄. Evaporation of the solvent under reduced pressure and purification of the residue on a silica gel column using EtOAc-hexane (1:4) as eluent furnished the compound 21 (16 g, 91 %) as white crystalline solid.

**RF = 0.4 (EtOAc-hexane 1:4); IR (neat) : νₜₓ/cm⁻¹ 2958, 1736, 1448, 1176 (0-C=O), 787, 571; ¹H NMR (200 MHz, CDCl₃): δ 8.02-7.84 (m, 3H), 7.57-7.06 (m, 7H), 4.32 (t, J = 6.95, 2H), 3.0 (t, J = 6.95, 2H), 2.03 (s, 3H); ¹³C NMR (50 MHz, CDCl₃): δ 170.9, 138.1, 135.1, 133.7, 130.7, 129.2, 126.6, 124.8, 123.4, 123.2, 119.3, 118.9, 115.6, 63.1, 24.4, 20.9; HRMS -ESI: calcd for C₇₃H₇₇NO₄[S] [M+ Na⁺] 366.0776; found: 366.0759.
Example 30: Synthesis of compound 22

To a cold (-78 °C) stirred solution of the indole 21 (200 ml) was added MeOCHCl (38.8 ml, 437.3 mmol) and SnC (51.2 ml, 437.3 mmol). The reaction mixture was allowed to come to -10 °C slowly over a period of 1 h and was poured into HCl (1M 500 ml). It was then extracted with CH$_2$Cl$_2$, washed with brine and dried over Na$_2$SO$_4$. Evaporation of the solvent and recrystallisation of the crude product from 1,2-dichloroethane furnished the aldehyde 22 (26 g, 80%) as a white solid.

\[ \text{RF} = 0.4 \text{ (EtOAc-hexane 2:8); IR (neat): } v_{max}/\text{cm}^{-1} 2923, 2853, 1738 \text{ (C=O), 1675 (C=O), 1543, 1448, 1175, 904, 724; } \]  
\[ ^1\text{H NMR (CDCl$_3$, 200 MHz): } 6.106 \text{ (s, 1H), 8.2 (d, } J = 8.5 \text{ Hz, 1H), 7.75-7.25 (m, 8H), 4.26 (t, } J = 6.7 \text{ Hz, 2H), 3.30 (t, } J = 6.7 \text{ Hz, 2H), 1.83 (s, 3H); } \]  
\[ ^{13}\text{C NMR (CDCl$_3$, 50MHz): } \delta 184.5, 170.5, 137.2, 136.5, 134.0, 133.2, 132.0, 130.0, 129.1, 128.9, 126.3, 124.7, 121.5, 115.6, 60.3, 24.2, 20.5; \]  
\[ \text{HRMS: m/z calcd for } C_{19}H_{17}NO$_5$SNa [M+Na$^+$]: 394.0725; found: 394.0725. \]

Example 31: Synthesis of compound 23

In THF (600 ml) was added a solution of LiOH (4.6 g, 202.2 mmol) in water (150 ml) and stirred magnetically for 3 h at RT. The reaction mixture was extracted with ethyl acetate, washed with brine and dried over Na$_2$SO$_4$. Evaporation of the solvent gave the crude alcohol 22' which was used in next step without further purification. To a cold (0 °C) solution of the crude alcohol 22' (12 g, 36.5 mmol) in CH$_2$Cl$_2$ (200 ml) was added imidazole (3.7 g, 54.7 mmol), TBSCI (7.1 g, 47.4 mmol) at 0°C and stirred magnetically for 6 h at RT. It was then extracted with CH$_2$Cl$_2$, washed with brine and dried over Na$_2$SO$_4$. Evaporation of the solvent and purification of the residue on a silica gel column using
EtOAc-hexane (1:19) as eluent furnished the compound 23 (16 g, 81%, over 2 steps) as a white crystalline solid; 

$R_t = 0.4$ (EtOAc-hexane 1:19); IR (neat): $\nu_{max}/cm^{-1}$ 2928, 1674 (C=O), 1448, 1368, 1174, 1089, 753, 595; $^1$H NMR (CD$_3$CN, 200 MHz): $\delta$ 10.46 (s, 1H), 8.1 (dt, $\gamma = 8.5$ and 0.8 Hz, 1H), 7.75-7.20 (m, 8H), 3.75 (t, $J = 6.2$ Hz, 2H), 3.08 (t, $J = 6.2$ Hz, 2H), 0.86 (s, 9H), -0.24 (s, 6H); $^1^3$C NMR (CD$_3$CN): $\delta$ 183.8, 136.7, 136.1, 134.1, 133.6, 128.9, 128.7, 126.2, 124.2, 122.3, 116.8, 114.9, 62.3, 27.6, 24.7, -4.6, -6.7.

Example 32: Synthesis of compound 23'

To a stirred solution of the aldehyde 23 (15 g, 33.9 mmol) in CH$_2$Cl$_2$ (150 ml) was added stabilised two carbon Wittig salt (17.7 g, 50.8 mmol) [prepared from Ph$_3$P (50 g, 190.0 mmol), ethyl bromoacetate (21.1 ml, 190.0 mmol) and toluene (300 ml)]. The reaction mixture was stirred for 6 h at RT. Evaporation of the solvent under reduced pressure and purification of the residue on a silica gel column using EtOAc-hexane (1:19) as eluent furnished the ester 23' (16 g, 91%) as white crystalline solid;

$R_t = 0.5$ (EtOAc-hexane 1:9); IR (neat): $\nu_{max}/cm^{-1}$ 2929, 2856, 1711 (0-C=O), 1630, 1174, 751, 577; $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 8.37-7.29 (m, 10H), 6.52 (d, $J = 16$Hz, 1H), 4.39 (q, $J = 14.3$, 7.2 Hz, 2H), 3.91 (t, $J = 6.2$ Hz, 2H), 3.04 (t, $J = 6.4$ Hz, 2H), 1.45 (t, $J = 7.2$ Hz, 3H), 0.85 (s, 9H), -0.1 (s, 6H); $^1^3$C NMR (CDCl$_3$, 50MHz): $\delta$ 166.3, 137.8, 137.0, 133.8, 133.7, 132.9, 130.8, 128.9, 126.6, 126.2, 124.5, 123.9, 122.5, 120.1, 115.2, 62.6, 60.6, 28.5, 25.8, 18.1, 14.2, -5.6; HRMS: m/z calcd for C$_{22}$H$_{33}$NO$_5$SiNa [M+Na$^+$]: 536.1903; found: 536.1909.

Example 33: Synthesis of compound 24

To a magnetically stirred solution of methylmagnesium iodide, [prepared from magnesium turnings (6.4 g,
29.2 mmol), methyl iodide (18.2 ml, 292.4 mmol) and few crystals of iodine in anhydrous ether (50 ml)] was added slowly a mixture of the ester 23' (15 g, 269.1 mmol) in anhydrous ether (50 ml). The reaction mixture was stirred for 2 h at RT. It was then quenched with aqueous NH₄Cl solution (50 ml), extracted with ethyl acetate (3 x 15 ml), washed with brine and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc-hexane (3:7) as eluent furnished the alcohol 24 (13 g, 89%) as a white solid;

Rf = 0.35 (EtOAc-hexane 1:3); IR (neat): ν_m/m/cm⁻¹ 3547 (OH), 2927, 1449, 1356, 1109, 751, 577; ¹H NMR (CDCl₃, 200 MHz): δ 8.35 (dt, J = 8.3 Hz, 1.1 Hz, 1H), 7.84 (dt, J = 7.1, 1.5 Hz, 2H), 7.64-7.28 (m, 6H), 7.06 (d, J = 16.2 Hz, 1H), 6.28 (d, J = 16.2 Hz, 1H), 3.91 (t, J = 6.7 Hz, 2H), 3.01 (t, J = 6.8 Hz, 2H), 1.63 (s, 6H), 0.9 (s, 9H), -0.05 (s, 6H); ¹³C NMR (CDCl₃, 100 MHz): δ 144.1, 138.3, 136.1, 135.0, 133.4, 131.1, 128.7, 126.5, 124.7, 123.5, 119.4, 116.5, 114.8, 71.0, 62.7, 29.6, 28.4, 25.8, 18.1, 5.5; HRMS: m/z calcd for C₇H₇NO₃SiK: 522.2110; found: 522.2100.

**Example 34: Synthesis of compound 18**

To a mixture of the compound 24 (5 g, 10 mmol) in anhydrous methanol (50 ml) was added Na₃P(O)₄ (5.7 g, 40.2 mmol) and Na-Hg (9.2 g, 40.2 mmol). The reaction mixture was stirred for 1 h at RT until all the amalgam had converted into liquid mercury. Water (20 ml) was added to the reaction mixture, extracted with ether (3 x 15 ml), washed with brine (20 ml) and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc-hexane (3:7) as eluent furnished the alcohol 18 (3.5 g, 97%) as a yellow solid;

Rf = 0.3 (EtOAc-hexane 3:7); IR (neat): ν_m/m/cm⁻¹ 3455 (OH), 3361 (NH), 3058, 2929, 1462, 1255, 1092, 793; ¹H NMR (CD₃CN, 400 MHz): δ 9.11 (br s, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.16 (d, J = 8 Hz, 1H), 6.97 (t, J = 7 Hz, 1H), 6.86 (t, J = 7.3 Hz, 1H), 6.56 (d, J = 16.3 Hz, 1H), 6.12 (d, J = 16.3 Hz, 1H), 3.66 (t, J = 7 Hz, 2H), 2.84 (t, J = 7 Hz, 2H), 2.80 (br s, 1H), 1.23 (s, 6H), 0.71 (s, 9H), -0.18 (s, 6H); ¹³C NMR (CD₃CN, 50 MHz): δ 136.4, 136.1, 132.8, 128.5, 121.8, 118.5, 118.2, 116.9, 114.5, 111.0, 110.1, 69.7, 63.1, 29.0, 27.2, 25.0, 17.6, 6.4; HRMS: m/z calcd for C₂₁H₁₅N₂O₂SiNa[M+Na⁺]: 398.1918; found: 398.1931.

**Example 35: Synthesis of compound 19**
To a cold (-78 °C), magnetically stirred solution of the alcohol 24 (5 g, 10 mmol) and dry Et₃N (8.3 ml, 60.24 mmol) in anhydrous THF (50 ml) was added MsCl (2 ml, 26 mmol). The reaction mixture was slowly allowed to warm to RT for 1.5 h and refluxed for 30 min. The precipitate formed was filtered using ethyl acetate. Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc-hexane (1:19) as eluent furnished the diene 19 (4.7 g, 81%) as a white crystalline solid;

\[ RF = 0.5 \text{ (EtOAc-hexane 1:19); IR (neat): } \nu_{\text{vap}}/\text{cm}^{-1} 3068, 2954, 2857, 1603, 1449, 1376, 1173, 1091, 748, 579; ^1H NMR (CDCl}_3, 200 MHz): \delta 8.23 (dt, J = 8.2, 1.01 Hz, 1H), 7.71-7.16 (m, 8H), 6.98 (d, J = 16.2 Hz, 1H), 6.62 (d, J = 16.3 Hz, 1H), 5.14 (d, J = 5.9 Hz, 2H), 3.8 (t, J = 6.8 Hz, 2H), 2.93 (t, J = 6.9 Hz, 2H), 2.07 (s, 3H), 0.78 (s, 9H), -0.17 (s, 6H); ^13C NMR (CDCl}_3, 50 MHz): \delta 142.1, 138.3, 137.0, 136.4, 135.7, 133.4, 131.3, 128.8, 126.6, 124.8, 123.6, 119.6, 119.4, 118.9, 118.3, 115.1, 62.7, 28.6, 25.8, 18.5, 18.2, -5.5; HRMS: m/z calcd for C_{27}H_{33}NO_3Si+[M+H]^+: 482.2185; found: 482.2178.\n
Example 36: Synthesis of compound 25a and 25b
To a solution of the alcohol 18 (200 mg, 0.55 mmol) and diene 19 (268 mg, 0.55 mmol) in anhydrous CH₂Cl₂ (12 ml) was added Cu(OTf)₂ (40 mg, 0.11 mmol). The resulting purpleish red solution was stirred for 0.5 h at RT. Aq. NaHCO₃ (10 ml) was added to the reaction mixture, extracted with CH₂Cl₂, washed with brine and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:49) as eluent furnished the dimer 25a, b (290 mg, 62%) as white crystalline solid;

Rf = 0.35 (EtOAc-hexane 1:49); IR (neat) : ν_max/cm⁻¹ 2928, 1471, 1453, 1377, 1253, 1173, 1090, 835, 741, 578; ¹H NMR (CDCl₃, 500 MHz) for 26b (major isomer) : δ 8.15 (d = 6.4 Hz, 1H), 7.44-7.18 (m, 7H), 7.11-6.93 (m, 4H), 5.32 (d, J = 9.3 Hz, 2H), 4.38 (dd, 9.1, 17.2 Hz, 1H), 3.81-3.64 (m, 4H), 2.97-2.78 (m, 5H), 2.30 (dt, J = 3.15, 9.5 and 12.5 Hz, 1H), 2.00 s (3H), 1.82-1.80 (m, 6H), 1.59 (s, 2H), 0.86 (s, 9H), 0.74 (s, 9H), 0.00 (s, 6H), -0.25 (s, 6H); ¹³C NMR (CDCl₃, 50 MHz) : δ 143.7, 138.6, 138.3, 136.0, 134.4, 133.8, 133.3, 131.5, 130.9, 128.9, 126.4, 124.8, 124.7, 123.4, 120.3, 119.4, 119.2, 118.8, 118.7, 118.3, 114.7, 110.2, 103.0, 64.1, 63.7, 62.7, 51.2, 34.9, 28.5, 27.7, 26.0, 25.8, 25.5, 18.4, 18.1, -5.2, -5.6; HRMS : m/z calcd for C₂₀H₁₈N₂O₃S₂Na [M+Na⁺] : 823.4360; found : 823.4359.

Example 37: Synthesis of compound 26a and 26b

To a solution of the alcohol 18 (100 mg, 0.27 mmol) and diene 19 (134 mg, 0.27 mmol) in anhydrous CH₂Cl₂ (10 ml) was added BF₃·OEt₂ (150 mg, 1.05 mmol). The resulting purplish red solution was stirred for 0.5 h at RT. Aq. NaHCO₃ (10 ml) was added to the reaction mixture, extracted with CH₂Cl₂, washed with brine and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (2:3) as eluent furnished the diol 26a, b (130 mg, 78%) as yellow crystalline solid; small portion of diols 26a, b (20mg) was purified by preparative TLC for data collection.

Rf = 0.35 (EtOAc-hexane 1:1); IR (neat) : ν_max/cm⁻¹ 3401 (OH), 2929, 1613, 1454, 1367, 1172, 1043, 751, 586; ¹H NMR (CDCl₃, 500 MHz) for 26b (major isomer) : δ 8.15 (d, J =
8.2 Hz, 1H), 7.65-7.03 (m, 12H), 6.21 (d, J = 16.2 Hz, 1H), 6.13 (d, J = 15.9 Hz, 1H), 5.29 (d, J = 9.8 Hz, 1H), 4.39 (q, J = 17.1 Hz, 1H), 3.81 (t, J = 6.1 Hz, 2H), 3.71-3.63 (m, 2H), 3.00-2.91 (m, 2H), 2.85-2.83 (m, 1H), 2.80 (t, J = 6.7 Hz, 2H), 2.39-2.29 (m, 1H), 2.05 (s, 3H), 1.82 (d, J = 4 Hz, 6H); \(^{13}C\) NMR (CDCl\(_3\), 125 MHz): \(\delta\) 144.3, 138.8, 137.9, 136.2, 134.8, 134.1, 133.5, 133.3, 130.7, 128.9, 126.3, 125.1, 124.4, 123.8, 120.5, 119.0, 118.8, 118.1, 115.1, 110.2, 103.0, 64.0, 63.1, 62.0, 50.8, 34.9, 28.2, 27.2, 25.7, 25.4, 18.1; HRMS: m/z calcd for C\(_{36}\)H\(_{38}\)N\(_2\)O\(_5\) [M+H\(^+\)]: 595.2631; found: 595.2621.

Example 38: Synthesis of compound 27a and 27b

To a solution of the alcohol 26a,b (90 mg, 0.15 mmol) in ethyl acetate (10 ml) was added IBX (254 mg, 0.90 mmol) and refluxed for 1 h. Aq. NaHCO\(_3\) was added to the reaction mixture and extracted with ethyl acetate (3 x 10 ml). The organic extract was washed with brine and dried over Na\(_2\)SO\(_4\). Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc-hexane (1:4) as eluent furnished the dial 27a,b (75 mg, 84%) as a waxy solid;

\(R_f = 0.6\) (EtOAc-hexane 1:4); IR (neat): \(\nu_{\text{max}}/\text{cm}^{-1}\) 2928, 2851, 1726 (C=O), 1452, 1382, 1175, 785, 685, 591; \(^1\)H NMR (CD\(_3\)CN, 500 MHz): \(\delta\) 9.6 (s, 2H), 8.1 (d, J = 8.5 Hz, 1H), 7.56-6.98 (m, 12H), 6.07 (d, J = 16.2 Hz, 1H), 5.99 (d, J = 16.2 Hz, 1H), 5.26 (d, J = 9.5 Hz, 1H), 4.40 (q, J = 17.4 Hz, 1H), 3.78 (d, J = 4.2 Hz, 2H), 3.68 (d, J = 2.1 Hz, 2H), 2.87 (d, J = 12.5, 7.6 Hz, 1H), 2.36 (dd, J = 12.8, 10.1 Hz, 1H), 2.01 (s, 3H), 1.77 (d, J = 6.1 Hz, 6H); \(^{13}C\) NMR (CD\(_3\)CN, 100MHz): \(\delta\) 200.9, 200.1, 146.7, 141.0, 138.8, 137.1, 137.0, 135.9, 135.5, 134.5, 133.1, 132.0, 130.7, 127.7, 127.6, 126.8, 125.4, 125.1, 122.1, 120.8, 120.5, 119.7, 116.0, 115.5, 111.9, 98.1, 65.8, 51.7, 41.0, 39.6, 36.14, 26.13, 25.9, 18.7; HRMS: m/z calcd for C\(_{36}\)H\(_{38}\)N\(_2\)O\(_5\)Na [M+Na\(^+\)]: 591.2318; found: 591.2304.

Example 39: Synthesis of compound 28a and 28b

To a solution of 27a,b

NHMe\(_2\), NaCNBH\(_3\) AcOH, MeOH
RT, 12h, 91%
mixture of NHMe₂ (0.30 ml, 2.0 M soln, 0.60 mmol) and NaCNBH₃ (18.5 mg, 0.30 mmol) in MeOH (2 ml) and acetic acid (0.01 ml) was added a solution of the dialdehyde 27a, b (45 mg, 0.075 mmol) in MeOH (2 ml) and stirred for 12 h at RT. The reaction was quenched with a saturated solution of NaHCO₃ and extracted with ethyl acetate (2 x 5 ml), washed with brine and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on a silica gel column using MeOH-CH₂Cl₂ (1:9) as eluent furnished the compound 28a,b (45 mg, 91%) as white crystalline solid.

Example 40: Synthesis of flinderole B (2, Major) and flinderole C (3, Minor)

The mixture of the compound

anhydrous MeOH (20 ml), Na₂HPO₄ (200 mg, 1.6 mmol) and Na-Hg (368 mg, 1.6 mmol) was stirred for 1 h at RT. Water (20 ml) was added to the reaction mixture, extracted with ether (3 x 15 ml), washed with brine and dried over Na₂SO₄. Evaporation of the solvent and purification of the residue on a silica gel column using MeOH-CH₂Cl₂ (1:19) as eluent furnished the flinderole C (3, Minor isomer) (20 mg, 15%) as a colourless waxy solid.
1H NMR (DMSO-d6, 500 MHz): δ 11.01 (s, 1H), 7.45 (dd J = 9.8 and 6.4 Hz, 2H), 7.24 (dd, J = 8.8 and 9.4 Hz, 2H), 7.06 (ddj = 7.6 and 7.3 Hz, 1H), 6.94 (m, 3H), 6.61 (d, J = 16.2 Hz, 1H), 6.56 (d, J = 16.2 Hz, 1H), 7.24 (dd J = 8.8 and 9.4 Hz, 1H), 6.56 (d, J = 16.2 Hz, 1H), 5.26 (brdJ = 9.8, 1H), 4.33 (ddj = 9.5, 7.9 and 7.9 Hz, 1H), 2.84-2.68 (m, 5H), 2.37-2.28 (m, 4H), 2.21 (s, 6H), 2.15 (s, 6H), 1.83 (s, 3H), 1.74 (s, 3H), 1.73 (s, 3H); 13C NMR (DMSO-d6 125MHz): δ 142.7, 136.6, 132.8, 132.5, 132.1, 131.9, 131.0, 128.2, 125.7, 122.3, 119.9, 118.7, 118.6, 118.4, 118.4, 117.9, 113.2, 110.9, 110.0, 103.7, 63.0, 60.7, 51.2, 45.2, 45.1, 40.3, 34.9, 25.7, 23.3, 21.8, 21.7, 18.2; HRMS: m/z calcd for C34H42N2[M+H+]: 509.3644; found: 509.3656.

Flinderole C (10 mg) was treated with 0.5M solution of TFA in acetonitrile to obtain the TFA salt of flinderole C:

IR (neat): vmax/cm⁻¹ 3434, 2990, 2254, 2128, 1660, 1026, 825,762; 1H NMR (DMSO-d6, 500 MHz): δ 11.23 (s, 1H), 10.22 (b, 2H, TFA protons), 7.60 (d, J = 7.8 Hz, 1H), 7.58-7.56 (m, 1H), 7.36-7.29 (m, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.11 (dd, J = 7.8 and 7.8 Hz, 1H), 7.02-6.99 (m, 3H), 6.86 (d, J = 16.2 Hz, 1H), 6.66 (d, J = 16.2 Hz, 1H), 5.28 (brd, J = 9.6 Hz, 1H), 4.40 (dd, J = 9.6, 9.0 and 7.8 Hz, 1H), 3.29-2.19 (m, 5H), 3.11-3.05 (m, 1H), 2.96 (m, 2H), 2.87 (s, 6H), 2.86 (s, 6H), 2.73 (ddj = 12.6, 7.8 Hz, 1H), 2.33 (ddj = 12.6, 9.0 Hz, 1H), 1.86 (s, 3H), 1.80 (s, 3H), 1.74 (s, 3H); 13C NMR (DMSO-d6 125MHz): δ 142.9, 136.3, 133.3, 133.1, 132.2, 131.8, 130.6, 127.3, 124.3, 122.4, 120.1, 118.7, 118.4, 118.3, 118.1, 117.5, 110.7, 109.7, 108.9, 99.6, 62.7, 56.8, 56.6, 50.6, 42.1, 41.9, 41.8, 41.6, 34.5, 25.2, 22.2, 18.8, 18.4, 17.8.

Further elution of the column with MeOH-CH2Cl2 (1:9) gave the flinderole B (2, Major isomer) (89 mg, 62 %) as a white waxy solid.

1H NMR (DMSO-d6, 500 MHz): δ 10.9 (s, 1H), 7.48 (dd, J = 8.5 and 7.0 Hz, 1H), 7.39 (dd, J = 7.8 and 5.2 Hz, 2H), 7.25 (d, J = 8.1 Hz, 1H), 7.07-6.97 (m, 3H), 6.93-6.90 (m, 1H), 6.47 (d, J = 16.0 Hz, 1H), 5.87 (d, J = 16.0 Hz, 1H), 5.30 (brd, J = 9.6 Hz, 1H), 4.16 (ddj = 8.8 and 8.4 Hz, 1H), 2.79-2.73 (m, 3H), 2.61-2.45 (m, 4H), 2.42-2.36 (m, 1H), 2.32-2.37 (m, 1H), 2.23 (s, 6H), 2.20-2.09 (m, 2H), 2.03 (s, 6H), 1.95 (s, 3H), 1.79 (s, 3H); 13C NMR (DMSO-d6 125MHz): δ 142.9, 136.6, 132.7, 132.6, 131.8, 131.4, 131.1, 128.1, 125.2, 122.2, 120.2, 118.7, 118.5, 118.5, 118.4, 116.4, 112.7, 110.9, 110.3, 103.8, 63.8, 60.7, 60.4, 51.0, 45.1, 44.9, 34.5, 25.7, 25.5, 21.6, 21.5, 18.2; HRMS: m/z calcd for C48H44N2 [M+H+]: 599.3644; found: 599.3656.

Flinderole B (30 mg) was treated with 0.5M solution of TFA in acetonitrile to obtain the TFA salt of flinderole B:

IR (neat): vmax/cm⁻¹ 3229 (NH), 2931, 1613, 1455, 1345, 1040, 745, 661, 592; 1H NMR (DMSO-d6, 500 MHz): δ 11.19 (s, 1H), 10.37 (s, 1H, TFA proton), 10.26 (s, 1H, TFA proton), 7.60 (d, J = 7.8 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.25 (d, J = 7.8 Hz, 1H), 7.09 (dd, J = 7.8 and 7.8 Hz, 1H), 7.05 (dd, J = 7.8 and 7.8 Hz, 1H), 7.03 (dd, J = 7.8 and 7.8 Hz, 1H), 6.97 (dd, J = 7.8 and 7.8 Hz, 1H), 6.54 (d, J = 16.2 Hz, 1H), 6.34 (d, J = 16.2 Hz, 1H), 5.36 (d, J = 9.0 Hz, 1H), 4.28 (ddj = 9.0, 8.4 and 8.0 Hz, 1H), 3.29-3.22 (m, 1H), 3.13-3.04 (m, 3H), 3.01-2.88 (m, 6H), 2.86 (s, 6H), 2.75 (s, 6H), 2.32 (dd, J = 12.6 and 8.4 Hz, 1H), 1.96 (s, 3H), 1.83 (s, 3H), 1.80 (s, 3H); 13C NMR (DMSO-d6 125MHz): δ 143.5, 136.3, 133.2, 132.2, 132.0, 131.9, 130.9, 127.4, 124.5, 122.3, 120.3, 118.7, 118.5, 118.2, 118.2, 116.0, 110.7, 110.1, 108.5, 99.8, 63.4, 56.9, 56.6, 50.5, 42.1, 42.0,
Comparative table of the spectral characteristics of Synthetic Flinderole (B) and Natural Flinderole (B)

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<td>18.4</td>
<td>2.95 (m, 2H)</td>
<td>2.95 (m, 2H)</td>
</tr>
<tr>
<td>7'</td>
<td>99.7</td>
<td>99.6</td>
<td>3.08 (m)</td>
<td>3.08 (m)</td>
</tr>
<tr>
<td>8'</td>
<td>131.5</td>
<td>131.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9'</td>
<td>118.0</td>
<td>118.1</td>
<td>7.56 (m)</td>
<td>7.58-7.56 (m)</td>
</tr>
<tr>
<td>10'</td>
<td>118.5</td>
<td>118.7</td>
<td>7.00 (m)</td>
<td>7.02-6.99</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(m)</td>
</tr>
<tr>
<td>---</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>-------</td>
</tr>
<tr>
<td>11’</td>
<td>119.5</td>
<td>120.1</td>
<td>7.00 (m)</td>
<td>7.02-6.99 (m)</td>
</tr>
<tr>
<td>12’</td>
<td>109.6</td>
<td>109.7</td>
<td>7.29 (m)</td>
<td>7.36-7.29 (m)</td>
</tr>
<tr>
<td>13’</td>
<td>131.0</td>
<td>130.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14’</td>
<td>124.2</td>
<td>124.3</td>
<td>5.28 (br d, 9.6)</td>
<td>5.28 (br d, 9.6)</td>
</tr>
<tr>
<td>15’</td>
<td>133.4</td>
<td>133.3</td>
<td>1.86 (s)</td>
<td>1.86 (s)</td>
</tr>
<tr>
<td>16’</td>
<td>17.8</td>
<td>17.8</td>
<td>1.80 (s)</td>
<td>1.80 (s)</td>
</tr>
<tr>
<td>17’</td>
<td>25.2</td>
<td>25.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
We claim

1. Compounds of general formula I

![General Formula I](image)

wherein,

- \( R_1 \) is selected independently from -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_2 \) is selected independently from -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_3 \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_4 \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_5 \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_6 \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_7 \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_8 \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_9 \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_{10} \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_{11} \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_{12} \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,

- \( R_{13} \) is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (2-Nitrovinyl), -CO₂H, -Ph, -CH₂CH=CH₂,
R₄ is selected independently from -H, CH₃, -Ph, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I,
-CH₂OH, -CH₂OCH₃, -CH₂OBn, -CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₃CH₂NH₂,
-CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂, - (4-Fluorophenyl), -C₂H₅,
-CH₂CH=CH₂, -CH₂=CMe₂, -CH=CEt₂, -OCH₃, OCH₂CH₃, -OCH₂CH₂CH₃, -OH, -CHO, -CONH₂,
-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONHMe,
-CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂OCH₂H, -CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl),
-CH₂=CHC₂H₅, -CH₂=CHC₂H₅, -CH₂=CHC₂H₅, -CH₂=CHC₂H₅, -CH₂=CHC₂H₅, -CH₂=CHC₂H₅,
-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, -CH₂CONHMe,
-CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H,
-CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl), -CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl),
-CH₂=CHC₂H₅, -CH₂=CHC₂H₅, -CH₂=CHC₂H₅, -CH₂=CHC₂H₅, -CH₂=CHC₂H₅, -CH₂=CHC₂H₅,
-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, -CH₂CONHMe,
-CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H,
-CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl), -CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl),
-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, -CH₂CONHMe,
-CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H,
-CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl), -CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl),
-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, -CH₂CONHMe,
-CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H,
-CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl), -CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl),
-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, -CH₂CONHMe,
-CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H,
-CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl), -CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl),
-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, -CH₂CONHMe,
-CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H,
-CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl), -CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl),
-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, -CH₂CONHMe,
-CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H,
-CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl), -CH₂CO₂Me, -CH₂CO₂Et, - (2-Nitrovinyl),
-CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂, -CH₂CH₂CONH₂, -CH₂CONHMe,
-CH₂CONMe₂, -CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H,
R₇ represents -H, -CH₃, -COCH₃, -SO₂Ph, -(BOC), -(Ph-F), -(Bn), -(C₅H₁₀F), -(CO₂Et), -(MOM);
With the proviso, when
-CH₂CO₂Et, - (2-Nitrovinyl), -CH₂=CHCO₂H, -CH₂=CHCO₂Me, -CH₂=CHCO₂Et, -CH₂=CHCN, 
-COCONH₂, -COCONHMMe, -COCONMe₂, -CH₂CH₂CO₂H, -CONHNH₂, -CH₂CONHNH₂,
-COCONMe₂, -SH, -SC₂H₅, -SCH=CH₂, -CH₂CH₂CH₂CO₂H, -COCH₃, -COOCH₂CH₃,
OCOCH₂CH₂CH₃, -CH₂CO₂CH₂CH₃, -COCH₂Ph, -COCH₂Ph, -COCOCI,

R₁₁ represents \(-\text{H}, \text{CH}_3, \text{CH}_2\text{CH}_3, \text{Br}, \text{Cl}, \text{F}, \text{I}, \text{CH}_2\text{OH}, \text{CH}_2\text{OCH}_3, \text{CH}_2\text{OBn}, \)
-CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NMMe₂, -CH₂CH₂NMMe₂, -CH₂NH₂,
-CH₂NMMe₂, CH₂NMMe₂, \(\text{-(4-Fluorophenyl)}, -\text{CO}_2\text{H}, \text{-Ph}, -\text{CH}_2\text{CH}=\text{CH}_2, -\text{CH}=\text{CMe}_2, -\text{CH}=\text{CEt}_2, \)
-OCH₃, OCH₂CH₃, COCH₃, -OH, -CHO, -CONH₂, -CH₂CONH₂, -CH₂CONMe₂, -CH₂CONMe₂,
-CH₂CONH₂, -CH₂CONHNH₂, -COCONMe₂, -SH, -SC₂H₅, -SCH=CH₂, -CH₂CH₂CH₂CO₂H, -OCOCH₃, -OCOCH₂CH₃,
OCOCH₂CH₂CH₃, -CH₂CO₂CH₂CH₃, -CH₂CO₂CH₂CH₃, -COCH₂Ph, -COCH₂Ph, -COCOCI,

R₁₂ represents \(-\text{H}, \text{CH}_3, \text{CH}_2\text{CH}_3, \text{Br}, \text{Cl}, \text{F}, \text{I}, \text{CH}_2\text{OH}, \text{CH}_2\text{OCH}_3, \text{CH}_2\text{OBn}, \)
-CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NMMe₂, -CH₂CH₂NMMe₂, -CH₂NH₂,
-CH₂NMMe₂, CH₂NMMe₂, \(\text{-(4-Fluorophenyl)}, -\text{CO}_2\text{H}, \text{-Ph}, -\text{CH}_2\text{CH}=\text{CH}_2, -\text{CH}=\text{CMe}_2, -\text{CH}=\text{CEt}_2, \)
-OCH₃, OCH₂CH₃, COCH₃, -OH, -CHO, -CONH₂, -CH₂CONH₂, -CH₂CONMe₂, -CH₂CONMe₂,
-CH₂CONH₂, -CH₂CONHNH₂, -COCONMe₂, -SH, -SC₂H₅, -SCH=CH₂, -CH₂CH₂CH₂CO₂H, -OCOCH₃, -OCOCH₂CH₃,
OCOCH₂CH₂CH₃, -CH₂CO₂CH₂CH₃, -CH₂CO₂CH₂CH₃, -COCH₂Ph, -COCH₂Ph, -COCOCI,

With the proviso, when R₄ is as indicated herein below,

\[
\text{R}_4= \begin{array}{c}
\text{R}_5 \\
\text{R}_6 \\
\text{R}_7 \\
\text{R}_8 \\
\end{array}
\]

R₈ represents \(-\text{H}, \text{CH}_3, \text{CH}_2\text{CH}_3, \text{CH}_2\text{CH}_2\text{CH}_3, \text{Br}, \text{Cl}, \text{F}, \text{I}, \text{CH}_2\text{OH}, \text{CH}_2\text{OCH}_3, \text{CH}_2\text{OBn}, \)
-CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NMMe₂, -CH₂CH₂NMMe₂, -CH₂NH₂,
-CH₂NHMe, CH₂NMe₂, - (4-Fluorophenyl), -CO₂H, -Ph, -CH₂CH=CH₂, -CH=CHMe₂, -CH=CEt₂,
-OCH₃, OCH₂CH₃, -COCH₃, -OH, -CHO, -CONH₂, -CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂,
-CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H, -CH₂CO₂Me,
-CH₂CO₂Et, - (2-Nitrovinyl), -CH₂=CHC0₂H, -CH=CHC0₂Me, -CH=CHC0₂Et, -CH₂=CHCN,
-COCO₂H, -COCONH₂, -COCONHMe, -COCONMe₂, -CH₂CH₂CO₂H, -CONNH₂, -CH₂CONNH₂,
-COCONMe₂, -SH, -SC₂H₅, -SCH=CH₂, -CH₂CH₂CH₂CO₂H, -OCOCH₃, -OCOCH₂CH₃,
OCOCH₂CH₂CH₃, -CH₂CO₂CH₂CH₃, -OCOCH₂Ph, -COCH₂Ph, -COCOCl,
-OCO(CH₂)₆Me.

R₇ = -H, -CH₃, -COCH₃, -SO₂Ph, -(BOC), -(Ph-F), -(Bn), -(C₅H₁₀F), -(CO₂Et), -(MOM).

With the proviso, when

R₇ represents -H, -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn,
-CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂,
-CH₂NMe₂, CH₂NMe₂, - (4-Fluorophenyl), -CO₂H, -Ph, -CH₂CH=CH₂, -CH=CMe₂, -CH=CEt₂,
-CH₃, OCH₂CH₃, -COCH₃, -OH, -CHO, -CONH₂, -CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂,
-CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H, -CH₂CO₂Me,
-CH₂CO₂Et, - (2-Nitrovinyl), -CH₂=CHC0₂H, -CH=CHC0₂Me, -CH=CHC0₂Et, -CH₂=CHCN,
-COCO₂H, -COCONH₂, -COCONHMe, -COCONMe₂, -CH₂CH₂CO₂H, -CONNH₂, -CH₂CONNH₂,
-COCONMe₂, -SH, -SC₂H₅, -SCH=CH₂, -CH₂CH₂CH₂CO₂H, -OCOCH₃, -OCOCH₂CH₃,
OCOCH₂CH₂CH₃, -CH₂CO₂CH₂CH₃, -CH₂CO₂CH₂CH₃, -OCOCH₂Ph, -COCH₂Ph, -COCOCl,
-OCO(CH₂)₆Me;

R₈ represents -H, -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -Br, -Cl, -F, -I, -CH₂OH, -CH₂OCH₃, -CH₂OBn,
-CH₂OCH₂CH₃, -CH₂CH₂OH, -CH₂CH₂Br, -CH₂CH₂NH₂, -CH₂CH₂NHMe, -CH₂CH₂NMe₂, -CH₂NH₂,
-CH₂NMe₂, CH₂NMe₂, - (4-Fluorophenyl), -CO₂H, -Ph, -CH₂CH=CH₂, -CH=CMe₂, -CH=CEt₂,
-CH₃, OCH₂CH₃, -COCH₃, -OH, -CHO, -CONH₂, -CH₂CONH₂, -CH₂CONHMe, -CH₂CONMe₂,
-CH₂CH₂CONH₂, CH₂CH₂CONHMe, -CH₂CH₂CONMe₂, -CN, -CH₂CN, -CH₂CO₂H, -CH₂CO₂Me,
-CH₂CO₂Et, - (2-Nitrovinyl), -CH₂=CHC0₂H, -CH=CHC0₂Me, -CH=CHC0₂Et, -CH₂=CHCN,
-COCO₂H, -COCONH₂, -COCONHMe, -COCONMe₂, -CH₂CH₂CO₂H, -CONNH₂, -CH₂CONNH₂,
-COCONMe₂, -SH, -SC₂H₅, -SCH=CH₂, -CH₂CH₂CH₂CO₂H, -OCOCH₃, -OCOCH₂CH₃,
OCOCH₂CH₂CH₃, -CH₂CO₂CH₂CH₃, -CH₂CO₂CH₂CH₃, -OCOCH₂Ph, -COCH₂Ph, -COCOCl,
with the proviso, when $R_1$ is $-\text{CH}_2\text{CH}_2\text{NHMe}$, $R_2$ is $-\text{CH}=\text{CMe}_2$, $R_3$ is $-\text{H}$, $R_4$ is $\ldots\text{CH}_3$, $R_5$ is $-\text{CH}(_2\text{CH}_2\text{NHMe}$ and $R_7$ is $-\text{H}$.

$R_6$ is $-\text{CH}_2\text{CH}_2\text{NHMe}$ and $R_7$ is $-\text{H}$;

with the proviso, when $R_1$ is $-\text{CH}_2\text{CH}_2\text{NMe}_2$, $R_2$ is $-\text{CH}=\text{CMe}_2$, $R_3$ is $-\text{H}$, $R_4$ is $-\text{CH}_3$.

2. The compound as claimed in claim 1, wherein said compounds are useful as antimalarial compound.

3. A process for the preparation of Flinderole A-C and compounds of general formula I as claimed in claim 1 comprising the steps of:

a. reacting indole aldehyde ($1c'$) with $\text{Ph}_3\text{P}=-\text{CHC}0\text{Et}$ followed by reaction of the resultant ester with $\text{MeMgBr}$ to obtain tertiary alcohol ($1d'$);

$$
\begin{array}{c}
\text{CHO} \\
\text{SO}_2\text{Ph}
\end{array}
\begin{array}{c}
1c' \\
\end{array}
$$

b. mesylating tertiary alcohol ($1d'$) as obtained in step (a) followed by elimination to obtain sulphonated diene ($1b'$);

$$
\begin{array}{c}
\text{R}_1 \\
\text{R}_4
\end{array}
\begin{array}{c}
\text{R} \\
\text{SO}_2\text{Ph}
\end{array}
\begin{array}{c}
1b' \\
\end{array}
$$
c. desulfonylating (lb') as obtained in step (b) using methanolic NaOH to obtain desulphonated diene (le');

\[
\text{(le') } R = H
\]

d. desulfonylating alcohol (ld') as obtained in step (a) with sodium amalgam to obtain alcohol (la'); and

\[
\text{(la')}
\]

e. reacting alcohol (la') as obtained in step (d) optionally with sulphonated diene (lb') as obtained in step (b) or desulphonated diene (le') as obtained in step (c) in presence of Lewis acid and a non-polar solvent at temperature in the range of 25 to 32°C to obtain sulphonated or desulphonated compound of general formula 1;

f. desulfonylating sulphonated compound of general formula 1 as obtained in step (e) using methanolic NaOH to obtain desulphonated Flinderole A-C and compounds of general formula 1.

Flinderole A (R=H)  Flinderole C  General Formula 1

Flinderole B (R=H)

4. The process as claimed in claim 1, wherein Lewis acid used in step (e) is selected
from Cu(OTf)2 or BF₃·OEt₂.

5. The process for the preparation of compounds of general formula I as claimed in claim 1, optionally comprising dimerization of alcohol (Ia') and the said process comprising the steps of:

a. adding alcohol (Ia') with lewis acid with stirring for a period in the range of 50 to 70 minutes at temperature in the range of 25 to 32°C followed by adding water to obtain reaction mixture;

b. extracting the reaction mixture as obtained in step (a) with non-polar solvent, washing with brine, drying followed by evaporating the solvent;

c. purifying the residue on silica gel column using EtOAc-hexane (1:39) to obtain compound of general formula 1.

6. The process as claimed in claim 6, wherein Lewis acid used in step (a) is selected from Cu(OTf)₂ or BF₃·OEt₂.

7. A pharmaceutical composition for the treatment of malaria comprising compounds of general formula I optionally along with pharmaceutically acceptable excipients.

8. The compounds of general formula 1 useful as anti-malarial compound and process for the preparation thereof substantially as herein described with references of examples and drawing accompanying the specification.
Scheme 1

Flinderole A (1, R = H)
Flinderole B (2, R = CH₃)

Flinderole C (3)
Isoborverine (R=H)
Dimethylisoborverine (R=CH₃)

Scheme 2
Figure 1. Proposed stereochemical model for the [3 + 2] cycloaddition.

Scheme 5
(a) Cu(OTf)$_2$ (0.2 equiv.), CH$_2$Cl$_2$, RT, 30 min., 95%; (b) BF$_3$-OEt$_2$ (0.2 equiv.), CH$_2$Cl$_2$, RT, 20 min., 92%; (c) Na/Hg (4.0 equiv), Na$_2$HPO$_4$ (4.0 equiv), MeOH, RT, 1 h, 94%.
Scheme 6

5 (a) Ac₂O (5.0 equiv), DMAP (0.2 equiv), Pyridine (5.0 equiv), CH₂Cl₂, RT, 6 h, 91%; (b) Dichloromethyl methyl ether (5.0 equiv), stannic chloride (5.0 equiv), CH₂Cl₂, -78 to -10 °C, 1 h, 80%; (c) i. LiOH (5.0 equiv), H₂O, THF, RT, 3 h; ii. TBSCI (1.3 equiv), imidazole (1.5 equiv), CH₂Cl₂, 0 °C to RT, 6 h, 81% (over 2 steps); (d) i. Ph₃P=CHCO₂Et (1.5 equiv), CH₂Cl₂, RT, 6 h, 91%; ii. Mel (10 equiv), Mg turnings (9 equiv), I₂ (cat.), Et₂O, 0 °C to RT, 2 h, 89%; (e) Na/Hg (4.0 equiv), Na₃HPO₄ (4.0 equiv), MeOH, RT, 1 h, 97%; (f) MsCl (3.0 equiv), Et₃N (6.0 equiv), THF, 0 °C to reflux, 2 h, 81%. (g) Cu(OTf)₂ (0.2 equiv), CH₂Cl₂, RT, 30 min, 62%. (h) BF₃·OEt₂ (4.0 equiv), CH₂Cl₂, RT, 30 min. 78%; (i) IBX (6.0 equiv), EtOAc, reflux, 1 h, 84%; (j) NHMe₂ (4.0 equiv), NaCNBH₃ (4.0 equiv), AcOH (cat.), MeOH, RT, 12 h, 91%; (k) Na/Hg (4.0 equiv), Na₃HPO₄ (4.0 equiv), MeOH, RT, 1 h, 2 (62%), 3 (15%).
INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2011/000899

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D 487/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<td>A</td>
<td>page 331, left-hand column, line 11 - page 331, right-hand column, line 7; Figure 1</td>
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Date of the actual completion of the international search
20 March 2012

Date of mailing of the international search report
05/04/2012

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Authorized officer
Usueli Ambrogi
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