Diastereoselective Syntheses of New Analogues of the Farnesyltransferase

Inhibitor RPR 130401

Nicolas Pichon[†], Anne Harrison-Marchand[†], Patrick Mailliet[‡] and Jacques Maddaluno^{,†}*

Laboratoire des Fonctions Azotées et Oxygénées Complexes de l'IRCOF, UMR 6014 CNRS, INSA and Université de Rouen, 76821 Mont St Aignan,
France, and Aventis, Centre de Recherche de Vitry-Alfortville, 13 quai Jules Guesde, 94403 Vitry-sur-Seine Cedex, France

Supporting Information

Table of Contents :

General Informations	S2
Compound 8 : IR	S3
Compound 8 : ^1H NMR (300 MHz)	S4
Compound 8 : ^1H NMR (300 MHz) blow-up	S5
Compound 8 : ^{13}C NMR (75 MHz)	S6
Compound 8 : ^{13}C NMR (75 MHz) blow-up 1	S7
Compound 8 : ^{13}C NMR (75 MHz) blow-up 2	S8
Compound 8 : ^{13}C NMR (75 MHz) blow-up 3	S9
Compound 15 : IR	S10
Compound 15 : ^1H NMR (300 MHz)	S11
Compound 15 : ^1H NMR (300 MHz) blow-up	S12
Compound 15 : ^{13}C NMR (75 MHz)	S13
Compound 17a : IR	S14
Compound 17a : ^1H NMR (300 MHz)	S15
Compound 17a : ^1H NMR (300 MHz) blow-up	S16
Compound 17a : ^{13}C NMR (75 MHz)	S17
Compound 17a : ^{13}C NMR (75 MHz) blow-up	S18
Compound 17b : IR	S19
Compound 17b : ^1H NMR (300 MHz)	S20
Compound 17b : ^{13}C NMR (75 MHz)	S21
Compound 17b : ^{13}C NMR (75 MHz) blow-up	S22
Compound 19a : IR	S23
Compound 19a : ^1H NMR (300 MHz)	S24
Compound 19a : ^1H NMR (300 MHz) blow-up	S25
Compound 19a : ^{13}C NMR (75 MHz)	S26
Compound 5a : IR	S27
Compound 5a : ^1H NMR (300 MHz)	S28
Compound 5a : ^1H NMR (300 MHz) blow-up 1	S29
Compound 5a : ^1H NMR (300 MHz) blow-up 2	S30
Compound 5a : ^{13}C NMR (75 MHz)	S31
Compound 5a : ^{13}C NMR (75 MHz) blow-up	S32

General Aspects. NMR spectra were recorded at room temperature on spectrometers operating at 300 or 200 MHz (^1H) and 75 or 50 MHz (^{13}C). Chemical shifts (δ) are given in parts per million (ppm) and the coupling constants (J) in hertz. The solvent was deuteriochloroform. IR spectra were obtained by transmission on a FTIR spectrometer. The mass spectra were obtained either under electron impact conditions (EI) at 70 eV ionizing potential or fast atom bombardment (FAB) by a Xe beam accelerated under 4 kV (current threshold = 10 mA) on a glycerol or 3-nitrobenzyl alcohol matrix. Melting points were determined using a microscope apparatus. Thin layer chromatography (TLC) was carried out on fluorescent plates. The silica gel used for flash chromatography²⁴ was 0.040-0.063 mm. All reagents were of reagent grade and were used as such or distilled prior to use. The presence of rotamers being noticed for compounds 16, 17, 9, 10 and 5, some NMR signals (^1H and ^{13}C) may be doubled. In this case, both chemical shifts have been indicated.

Compound 6: ¹H NMR (500 MHz)

Chemical structure of Compound 6: COC(=O)C1=CC=C(C=C1)C2=CC=C(C=C2)C3=CC=C(C=C3)C4=CC=C(C=C4)C5=CC=C(C=C5)C6=CC=C(C=C6)C7=CC=C(C=C7)C8=CC=C(C=C8)C9=CC=C(C=C9)C10=CC=C(C=C10)C11=CC=C(C=C11)C12=CC=C(C=C12)C13=CC=C(C=C13)C14=CC=C(C=C14)C15=CC=C(C=C15)C16=CC=C(C=C16)C17=CC=C(C=C17)C18=CC=C(C=C18)C19=CC=C(C=C19)C20=CC=C(C=C20)C21=CC=C(C=C21)C22=CC=C(C=C22)C23=CC=C(C=C23)C24=CC=C(C=C24)C25=CC=C(C=C25)C26=CC=C(C=C26)C27=CC=C(C=C27)C28=CC=C(C=C28)C29=CC=C(C=C29)C30=CC=C(C=C30)C31=CC=C(C=C31)C32=CC=C(C=C32)C33=CC=C(C=C33)C34=CC=C(C=C34)C35=CC=C(C=C35)C36=CC=C(C=C36)C37=CC=C(C=C37)C38=CC=C(C=C38)C39=CC=C(C=C39)C40=CC=C(C=C40)C41=CC=C(C=C41)C42=CC=C(C=C42)C43=CC=C(C=C43)C44=CC=C(C=C44)C45=CC=C(C=C45)C46=CC=C(C=C46)C47=CC=C(C=C47)C48=CC=C(C=C48)C49=CC=C(C=C49)C50=CC=C(C=C50)C51=CC=C(C=C51)C52=CC=C(C=C52)C53=CC=C(C=C53)C54=CC=C(C=C54)C55=CC=C(C=C55)C56=CC=C(C=C56)C57=CC=C(C=C57)C58=CC=C(C=C58)C59=CC=C(C=C59)C60=CC=C(C=C60)C61=CC=C(C=C61)C62=CC=C(C=C62)C63=CC=C(C=C63)C64=CC=C(C=C64)C65=CC=C(C=C65)C66=CC=C(C=C66)C67=CC=C(C=C67)C68=CC=C(C=C68)C69=CC=C(C=C69)C70=CC=C(C=C70)C71=CC=C(C=C71)C72=CC=C(C=C72)C73=CC=C(C=C73)C74=CC=C(C=C74)C75=CC=C(C=C75)C76=CC=C(C=C76)C77=CC=C(C=C77)C78=CC=C(C=C78)C79=CC=C(C=C79)C80=CC=C(C=C80)C81=CC=C(C=C81)C82=CC=C(C=C82)C83=CC=C(C=C83)C84=CC=C(C=C84)C85=CC=C(C=C85)C86=CC=C(C=C86)C87=CC=C(C=C87)C88=CC=C(C=C88)C89=CC=C(C=C89)C90=CC=C(C=C90)C91=CC=C(C=C91)C92=CC=C(C=C92)C93=CC=C(C=C93)C94=CC=C(C=C94)C95=CC=C(C=C95)C96=CC=C(C=C96)C97=CC=C(C=C97)C98=CC=C(C=C98)C99=CC=C(C=C99)C100=CC=C(C=C100)C101=CC=C(C=C101)C102=CC=C(C=C102)C103=CC=C(C=C103)C104=CC=C(C=C104)C105=CC=C(C=C105)C106=CC=C(C=C106)C107=CC=C(C=C107)C108=CC=C(C=C108)C109=CC=C(C=C109)C110=CC=C(C=C110)C111=CC=C(C=C111)C112=CC=C(C=C112)C113=CC=C(C=C113)C114=CC=C(C=C114)C115=CC=C(C=C115)C116=CC=C(C=C116)C117=CC=C(C=C117)C118=CC=C(C=C118)C119=CC=C(C=C119)C120=CC=C(C=C120)C121=CC=C(C=C121)C122=CC=C(C=C122)C123=CC=C(C=C123)C124=CC=C(C=C124)C125=CC=C(C=C125)C126=CC=C(C=C126)C127=CC=C(C=C127)C128=CC=C(C=C128)C129=CC=C(C=C129)C130=CC=C(C=C130)C131=CC=C(C=C131)C132=CC=C(C=C132)C133=CC=C(C=C133)C134=CC=C(C=C134)C135=CC=C(C=C135)C136=CC=C(C=C136)C137=CC=C(C=C137)C138=CC=C(C=C138)C139=CC=C(C=C139)C140=CC=C(C=C140)C141=CC=C(C=C141)C142=CC=C(C=C142)C143=CC=C(C=C143)C144=CC=C(C=C144)C145=CC=C(C=C145)C146=CC=C(C=C146)C147=CC=C(C=C147)C148=CC=C(C=C148)C149=CC=C(C=C149)C150=CC=C(C=C150)C151=CC=C(C=C151)C152=CC=C(C=C152)C153=CC=C(C=C153)C154=CC=C(C=C154)C155=CC=C(C=C155)C156=CC=C(C=C156)C157=CC=C(C=C157)C158=CC=C(C=C158)C159=CC=C(C=C159)C160=CC=C(C=C160)C161=CC=C(C=C161)C162=CC=C(C=C162)C163=CC=C(C=C163)C164=CC=C(C=C164)C165=CC=C(C=C165)C166=CC=C(C=C166)C167=CC=C(C=C167)C168=CC=C(C=C168)C169=CC=C(C=C169)C170=CC=C(C=C170)C171=CC=C(C=C171)C172=CC=C(C=C172)C173=CC=C(C=C173)C174=CC=C(C=C174)C175=CC=C(C=C175)C176=CC=C(C=C176)C177=CC=C(C=C177)C178=CC=C(C=C178)C179=CC=C(C=C179)C180=CC=C(C=C180)C181=CC=C(C=C181)C182=CC=C(C=C182)C183=CC=C(C=C183)C184=CC=C(C=C184)C185=CC=C(C=C185)C186=CC=C(C=C186)C187=CC=C(C=C187)C188=CC=C(C=C188)C189=CC=C(C=C189)C190=CC=C(C=C190)C191=CC=C(C=C191)C192=CC=C(C=C192)C193=CC=C(C=C193)C194=CC=C(C=C194)C195=CC=C(C=C195)C196=CC=C(C=C196)C197=CC=C(C=C197)C198=CC=C(C=C198)C199=CC=C(C=C199)C200=CC=C(C=C200)C201=CC=C(C=C201)C202=CC=C(C=C202)C203=CC=C(C=C203)C204=CC=C(C=C204)C205=CC=C(C=C205)C206=CC=C(C=C206)C207=CC=C(C=C207)C208=CC=C(C=C208)C209=CC=C(C=C209)C210=CC=C(C=C210)C211=CC=C(C=C211)C212=CC=C(C=C212)C213=CC=C(C=C213)C214=CC=C(C=C214)C215=CC=C(C=C215)C216=CC=C(C=C216)C217=CC=C(C=C217)C218=CC=C(C=C218)C219=CC=C(C=C219)C220=CC=C(C=C220)C221=CC=C(C=C221)C222=CC=C(C=C222)C223=CC=C(C=C223)C224=CC=C(C=C224)C225=CC=C(C=C225)C226=CC=C(C=C226)C227=CC=C(C=C227)C228=CC=C(C=C228)C229=CC=C(C=C229)C230=CC=C(C=C230)C231=CC=C(C=C231)C232=CC=C(C=C232)C233=CC=C(C=C233)C234=CC=C(C=C234)C235=CC=C(C=C235)C236=CC=C(C=C236)C237=CC=C(C=C237)C238=CC=C(C=C238)C239=CC=C(C=C239)C240=CC=C(C=C240)C241=CC=C(C=C241)C242=CC=C(C=C242)C243=CC=C(C=C243)C244=CC=C(C=C244)C245=CC=C(C=C245)C246=CC=C(C=C246)C247=CC=C(C=C247)C248=CC=C(C=C248)C249=CC=C(C=C249)C250=CC=C(C=C250)C251=CC=C(C=C251)C252=CC=C(C=C252)C253=CC=C(C=C253)C254=CC=C(C=C254)C255=CC=C(C=C255)C256=CC=C(C=C256)C257=CC=C(C=C257)C258=CC=C(C=C258)C259=CC=C(C=C259)C260=CC=C(C=C260)C261=CC=C(C=C261)C262=CC=C(C=C262)C263=CC=C(C=C263)C264=CC=C(C=C264)C265=CC=C(C=C265)C266=CC=C(C=C266)C267=CC=C(C=C267)C268=CC=C(C=C268)C269=CC=C(C=C269)C270=CC=C(C=C270)C271=CC=C(C=C271)C272=CC=C(C=C272)C273=CC=C(C=C273)C274=CC=C(C=C274)C275=CC=C(C=C275)C276=CC=C(C=C276)C277=CC=C(C=C277)C278=CC=C(C=C278)C279=CC=C(C=C279)C280=CC=C(C=C280)C281=CC=C(C=C281)C282=CC=C(C=C282)C283=CC=C(C=C283)C284=CC=C(C=C284)C285=CC=C(C=C285)C286=CC=C(C=C286)C287=CC=C(C=C287)C288=CC=C(C=C288)C289=CC=C(C=C289)C290=CC=C(C=C290)C291=CC=C(C=C291)C292=CC=C(C=C292)C293=CC=C(C=C293)C294=CC=C(C=C294)C295=CC=C(C=C295)C296=CC=C(C=C296)C297=CC=C(C=C297)C298=CC=C(C=C298)C299=CC=C(C=C299)C300=CC=C(C=C300)C301=CC=C(C=C301)C302=CC=C(C=C302)C303=CC=C(C=C303)C304=CC=C(C=C304)C305=CC=C(C=C305)C306=CC=C(C=C306)C307=CC=C(C=C307)C308=CC=C(C=C308)C309=CC=C(C=C309)C310=CC=C(C=C310)C311=CC=C(C=C311)C312=CC=C(C=C312)C313=CC=C(C=C313)C314=CC=C(C=C314)C315=CC=C(C=C315)C316=CC=C(C=C316)C317=CC=C(C=C317)C318=CC=C(C=C318)C319=CC=C(C

Compound 8: ^1H NMR (300 MHz) blow-up

Compound 8: ^{13}C NMR (75 MHz)

Compound 8: ^{13}C NMR (75 MHz) blow-up 1

Compound 8: ^{13}C NMR (75 MHz) blow-up 2

Compound 8: ^{13}C NMR (75 MHz) blow-up 3

Compound 15: ^1H NMR (300 MHz)

Compound 15: ^1H NMR (300 MHz) blow-up

Compound 15: ^{13}C NMR (75 MHz)

Compound 17a: IR

Chemical structure of compound 10 (•syn) is shown in the top right corner. The structure is a complex polycyclic molecule with a benzene ring, a cyclohexane ring, and a nitrogen-containing side chain with an ester group.

Compound 17a: ^1H NMR (300 MHz) blow-up

Compound 17a: ^{13}C NMR (75 MHz)

Compound 17a: ^{13}C NMR (75 MHz) blow-up

Compound 17b: RMN ^1H (300 MHz)

Compound 17b: RMN ^{13}C (75 MHz)

Compound 17b: RMN ^{13}C (75 MHz) blow-up

Compound 19a: RMN ^1H (300 MHz) blow-up

Compound 19a: RMN ^{13}C (75 MHz)

Compound 5a: IR

Compound 5a: RMN ^1H (300 MHz)

Compound 5a: RMN ^1H (300 MHz) blow-up 2

Compound 5a: RMN ^{13}C (75 MHz)

Compound 5a: RMN ^{13}C (75 MHz) blow-up