Synthesis of the Gymnodimine Tetrahydrofuran Core.

Sylvestre Tounieux, a Redouane Beniazza, a Valérie Desvergnes, a Romulo Araoz, b Jordi Molgo, b and Yannick Landais a *

a, University of Bordeaux, Institut des Sciences Moléculaires, UMR-CNRS-5255, 351 cours de la libération, 33405 Talence, Cedex, France

b, Institut Fédératif de Neurobiologie Alfred Fessard
Laboratoire de Neurobiologie et Développement, UPR 3294
1, Avenue de la Terrasse, Bâtiments 32-33,
91198-Gif sur Yvette cedex, France

c, Present address: Laboratoire des Glucides UMR-CNRS 6219, Université de Picardie Jules Verne, 33 Rue Saint Leu, 80 039 AMIENS, France

Supporting information

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General Considerations:

$^1$H NMR and $^{13}$C NMR were recorded on a Bruker AC-250 FT ($^1$H: 250 MHz, $^{13}$C: 62.9 MHz), Bruker Avance-300 FT ($^1$H: 300 MHz, $^{13}$C: 75.46 MHz), and Bruker DPX-400 FT ($^1$H: 400 MHz, $^{13}$C: 100.6 MHz) using CDCl$_3$ as internal reference unless otherwise indicated. The chemical shifts ($\delta$) and coupling constants ($J$) are expressed in ppm and hertz respectively. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, m = multiplet, br = broad. IR spectra were recorded on a Perkin-Elmer Paragon 1000 FT-IR spectrophotometer as neat films on NaCl windows or as KBr pellets or using a diamond ATR accessory (Golden gate). HRMS were recorded on a Micromass ZABSpec TOF apparatus, on a Q-Tof Applied Biosystems and on Waters Q-Tof 2 apparatus (for ESI). Melting points were determined by using a Stuart scientific digital 7SMP3 apparatus and are uncorrected.

Merck silica gel (0.043-0.063 mm) was used for flash chromatography. All reactions were carried out under nitrogen or Argon atmosphere unless specified. CH$_2$Cl$_2$ and acetonitrile were distilled over CaH$_2$. THF and Et$_2$O were distilled from sodium/benzophenone prior to use. All commercially available reagent-grade chemicals were used as received, unless otherwise stated. Yields refer to chromatographically and spectroscopically ($^1$H NMR) homogeneous materials.

(E)-methyl 3-((2R,3R,5R)-5-(3-(tert-butyldimethylsilyloxy)propyl)-3-methyltetrahydrofuran-2-yl)but-2-enoate

To a solution of (E)-methyl 3-((2R,3R,5R)-5-(3-hydroxypropyl)-3-methyl-tetrahydrofuran-2-yl)but-2-enoate 10 (47 mg, 0.186 mmol) in DCM (3.6 ml) was added at RT, pyridine (65 µL, 0.465 mmol, 2.5 eq.), TBSCl (56 mg, 0.372 mmol, 2 eq.) and finally DMAP (4.5 mg, 0.037 mmol, 0.2 eq.). The clear solution was then stirred for 16h at RT (~ 15°C). The mixture was quenched by water, extracted with DCM (3x15 mL). The organic layers were combined and dried over MgSO$_4$, filtered and concentrated under reduced pressure. Purification on silica gel (PE/EA: 98/2 to 95/5) provided the (E)-methyl 3-((2R,3R,5R)-5-allyl-3-methyl-tetrahydrofuran-2-yl)but-2-enoate as a colorless oil (47 mg, 71%).

$[\alpha]D^0 = -12.6$ (C = 0.22 , CHCl$_3$)

IR (film, NaCl): $\nu$(cm$^{-1}$) = 2957, 2861, 1722, 1655, 1159, 1096
$^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ (ppm) = 5.91-5.86 (m, 1 H), 4.09-3.97 (m, 1 H), 3.78 (d, $J \sim 6.6$ Hz, 1 H), 3.71-3.58 (m, 2 H), 3.68 (s, 3H), 2.17-1.97 (m, 1 H), 2.11 (d, $J \sim 1.2$ Hz, 3H), 1.78-1.48 (m, 6 H), 1.05 (d, $J \sim 6.6$ Hz, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H).

$^{13}$C NMR (CDCl$_3$, 75.5 MHz): $\delta$ (ppm) = 167.3, 158.7, 114.9, 90.5, 78.8, 63.2, 51.0, 39.7, 38.3, 32.5, 29.6, 26.1, 18.5, 14.8, -5.2.

HRMS (ESI): [M+Na]$^+$ C$_{19}$H$_{36}$O$_4$Si Na: calcd. 379.22806, found 379.2283
Compound 2a CDCl$_3$ - 400 MHz
Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Compound 3a CDCl₃ - 100.6 MHz
Compound 4a  F1  CDCl3  300 MHz
Compound 4a  F1  CDCl3  75.5 MHz
Compound 4a  F2  CDCl3  300 MHz
Compound 4a  F2  CDCl3  75.5 MHz
compound 4b CDCl3  52.5 MHz
Compound 5a, CDCl₃, 75.5 MHz

![NMR spectrum of compound 5a](image)
Compound 5b   C6D6   600 MHz

![NMR spectrum of Compound 5b in C6D6 at 600 MHz](image)
Compound 5b  C6D6  150 MHz

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Compound 6  CDCl₃  75.5 MHz

EtO

OH
compound 7 CDCl₃ 300 MHz
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compound 7 CDCl₃ 75.5 MHz

\[\text{Diagram of compound 7 with chemical shifts and peaks.}\]

\[\text{Chart with f1 (ppm) on the x-axis and peaks at various ppm values.}\]
Compound 8  CDCl3  200 MHz
Compound 8  CDCl$_3$  52.5 MHz
Compound 9  CDCl₃  300 MHz
Compound 9  CDCl₃  75.5 MHz

![NMR spectrum of Compound 9](image)
compound 11 CDCl3 300 MHz
Compound 11  CDCl₃  75.5 MHz
Compound 12 CDCl₃ 300 MHz

OTES

H
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Compound 12  CDCl₃  75.5 MHz

O TBS  OH
CDCl₃, 75.5 MHz

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